# STIC Search Report
## Biotech-Chem Library

STIC Database Tracking Number: 133999

| | |
|---|---|
| **TO: Rebecca Cook**<br>**Location: REM-3C70**<br>**Art Unit: 1614**<br>**Monday, October 04, 2004**<br><br>**Case Serial Number: 10/694448** | **From: Mary Jane Ruhl**<br>**Location: Biotech-Chem Library**<br>**Remsen 1-A-62**<br>**Phone: 571-272-2524**<br><br>**maryjane.ruhl@uspto.gov** |

## Search Notes

Examiner Cook,

Here are the results for your recent search request.

Please feel free to contact me if you have any questions about these results.

Thank you for using STIC services. We appreciate the opportunity to serve you.

Sincerely,

Mary Jane Ruhl
Technical Information Specialist
STIC
Remsen 1-A-62
Ext. 22524

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=> d his ful

     FILE 'REGISTRY' ENTERED AT 11:17:16 ON 04 OCT 2004
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L1            1 SEA ABB=ON  L-METHIONINE/CN
                E D-METHIONINE/CN
L2            1 SEA ABB=ON  D-METHIONINE/CN
                E METHIONINE/CN
                E S-ADENOSYL-L-METHIONINE/CN
L3            1 SEA ABB=ON  S-ADENOSYL-L-METHIONINE/CN

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                L(W)?METHIONINE?

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L8              STR

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FILE 'HCAPLUS' ENTERED AT 11:33:10 ON 04 OCT 2004
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L15 6 SEA ABB=ON L14 AND (?OTOTOX? OR EAR? OR ?HEAR? OR ?OTOLOG? OR ?OTOLARYNG?)
L16 18 SEA ABB=ON L14 OR L15
L17 15 SEA ABB=ON L16 AND (?PATIENT? OR ?HUMAN? OR MAN? OR CAT? OR ?FELINE? OR DOG? OR ?CANINE?)
L18 18 SEA ABB=ON L16 OR L17
L19 18 SEA ABB=ON L18 AND (?PREVENT? OR ?TREAT? OR ?INHIBIT? OR ?SUPPRES? OR ?RESIST? OR ?THERAP? OR ?CONTROL? OR ?HEAL? OR ?MEDICIN? OR ?PHARM?)
L20 8 SEA ABB=ON L19 AND (?METHOD? OR ?TECHNIQ?)
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L31 20 SEA ABB=ON L27 OR L28 OR L29 OR L30
L32 38 SEA ABB=ON L21 OR L31
L33 26 SEA ABB=ON L32 AND (?OTOTOX? OR EAR? OR ?HEAR? OR ?OTOLOG? OR ?OTOLARYNG?)

26 cits from CA Plus, from structure/text search + text search

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L1             1 SEA FILE=REGISTRY ABB=ON  L-METHIONINE/CN
L2             1 SEA FILE=REGISTRY ABB=ON  D-METHIONINE/CN
L3             1 SEA FILE=REGISTRY ABB=ON  S-ADENOSYL-L-METHIONINE/CN
L4         93275 SEA FILE=HCAPLUS ABB=ON  L1 OR L2 OR L3 OR ?METHIONINE? OR
                 S(W)?ADENOSYL?(W)L(W)?METHIONINE?
L5             1 SEA FILE=REGISTRY ABB=ON  PLATINUM/CN
L6           511 SEA FILE=HCAPLUS ABB=ON  L4 AND (L5 OR PT OR ?PLATINUM?)
L7            18 SEA FILE=HCAPLUS ABB=ON  L6 AND (?CHEMOTHER? OR ?ANTI?(W)(?TUMO
                 R? OR ?TUMOUR?))
L8                 STR

                    7
                   G3              Ak~N~Ak
                   |                8  @9  10
H3C~G1~S~G2~CH~G4
  1   2   3   4   5   6

REP G1=(0-3) CH2
REP G2=(1-3) CH2
VAR G3=O/C
VAR G4=9/OH
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M1-X6 C  AT   8
ECOUNT  IS M1-X6 C  AT  10

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE
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            OR ?OTOLOG? OR ?OTOLARYNG?)
L16          18 SEA FILE=HCAPLUS ABB=ON  L14 OR L15
L17          15 SEA FILE=HCAPLUS ABB=ON  L16 AND (?PATIENT? OR ?HUMAN? OR MAN?
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L19          18 SEA FILE=HCAPLUS ABB=ON  L18 AND (?PREVENT? OR ?TREAT? OR
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L20           8 SEA FILE=HCAPLUS ABB=ON  L19 AND (?METHOD? OR ?TECHNIQ?)
L21          18 SEA FILE=HCAPLUS ABB=ON  L19 OR L20
L22             SEL  L6 1- RN :    7935 TERMS
L23        7935 SEA FILE=REGISTRY ABB=ON  L22
L25           2 SEA FILE=REGISTRY SUB=L23 SSS FUL L8
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L28          13 SEA FILE=HCAPLUS ABB=ON  L27 AND (?PATIENT? OR ?HUMAN? OR MAN?
            OR CAT? OR ?FELINE? OR DOG? OR ?CANINE?)
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L30           3 SEA FILE=HCAPLUS ABB=ON  L27 AND (?METHOD? OR ?TECHNIQ?)
L31          20 SEA FILE=HCAPLUS ABB=ON  L27 OR L28 OR L29 OR L30
L32          38 SEA FILE=HCAPLUS ABB=ON  L21 OR L31
L33          26 SEA FILE=HCAPLUS ABB=ON  L32 AND (?OTOTOX? OR EAR? OR ?HEAR?
            OR ?OTOLOG? OR ?OTOLARYNG?)
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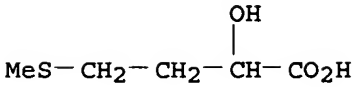
=> d ibib abs hitstr l33 1-26

L33 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:298909 HCAPLUS
DOCUMENT NUMBER: 141:70850
TITLE: Feeding 2-hydroxy-4-(methylthio)-butanoic acid to periparturient dairy cows improves milk production but not hepatic metabolism
AUTHOR(S): Piepenbrink, M. S.; Marr, A. L.; Waldron, M. R.; Butler, W. R.; Overton, T. R.; Vazquez-Anon, M.; Holt, M. D.
CORPORATE SOURCE: Department of Animal Science, Cornell University, Ithaca, NY, 14853, USA
SOURCE: Journal of Dairy Science (2004), 87(4), 1071-1084
CODEN: JDSCAE; ISSN: 0022-0302
PUBLISHER: American Dairy Science Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Holstein dairy cows (n=48) entering second or later lactation were used to determine the effects of 2-hydroxy-4-(methylthio)butanoic acid (HMB, methionine hydroxy analog) on milk production, hepatic lipid metabolism, and gluconeogenesis during the periparturient period. The cows were fed 3 diets as total mixed rations starting 21 days before expected calving. The diets contained 0 (basal diet), 0.09 (+HMB), or 0.18 (++HMB)% HMB. From parturition to 84 days in milk, the cows were fed diets with 0, 0.13, or 0.20% HMB. Prepartum and postpartum dry matter intakes were similar among cows fed the basal, +HMB, and ++HMB diets. There was a quadratic effect on milk yield such that cows fed +HMB had the greatest milk yield; yields of milk in cows fed the basal and ++HMB diets were similar. This led to trends for increased yields of 3.5% fat-corrected milk and total milk solids when cows were fed +HMB diet. The % of milk fat, protein, and total solids were not affected by dietary **treatments**. Despite differences in milk yield, the calculated energy balance was not affected by dietary **treatments**. Blood plasma concns. of nonesterified fatty acids, β-hydroxybutyrate, and glucose were not different among the **treatments**. Liver triglyceride contents were similar among **treatments** on day 1 postpartum and were increased in cows fed +HMB diet on day 21 postpartum compared to the other dietary **treatments**. The capacities for metabolism of [1-14C]palmitate by liver slices in vitro were not affected by **treatments**, but the conversion of [1-14C]propionate to CO2 and glucose decreased as the amount of HMB fed increased on day 21 postpartum. Cows fed +HMB had greater days-to-first ovulation compared with cows fed the basal and ++HMB diets as measured by blood plasma progesterone concns. Thus, adding HMB to low-methionine diets to achieve methionine level of .apprx.2.3% of metabolizable protein supply is beneficial for increasing milk production, but does not appear to benefit hepatic energy metabolism during **early** lactation.

IT **583-91-5**, 2-Hydroxy-4-(methylthio)-butanoic acid
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(dietary 2-hydroxy-4-(methylthio)butanoic acid (methionine hydroxy analog) improves milk production but not hepatic metabolism in periparturient Holstein dairy cows)

RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:220127 HCAPLUS
DOCUMENT NUMBER: 140:270109
TITLE: Use of metal chelates in **human** or animal feeding
INVENTOR(S): Cinti, Enrico; Ciribolla, Antonio
PATENT ASSIGNEE(S): Agristudio S.R.L., Italy
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004021802 | A2 | 20040318 | WO 2003-IT400 | 20030627 |
| WO 2004021802 | A3 | 20040415 | | |

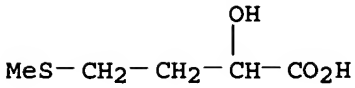
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2002-RE67 A 20020906
IT 2003-MI863 A 20030429

AB The present invention relates to the use in **human** and animal nutrition (monogastric and polygastric animals) of known chelates of bivalent metal Mg, Ca, Mn, Co, Cu, Zn and Fe with methionine hydroxy analog. The present invention further relates to a **method** for preparing new chelates with methionine hydroxy analog, both in solid form with iron (II), vanadium (IV) and (V) and molybdenum (V) and (VI), and in liquid form in aqueous solution with iron (II) and (III) and chrome (III). Eventually, the present invention relates to the use of said new chelates, both in solid form with iron (II), vanadium (IV) and (V) and molybdenum (V) and (VI), and in liquid form in aqueous solution with iron (II) and (III) and chrome (III), in **human** and animal nutrition.

IT **583-91-5DP**, metal complexes
RL: FFD (Food or feed use); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of metal chelates in **human** or animal feeding)

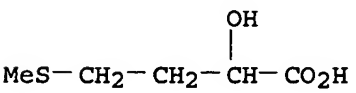
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:912094 HCAPLUS
DOCUMENT NUMBER: 140:145274
TITLE: Adaptations in body muscle and fat in transition dairy **cattle** fed differing amounts of protein and methionine hydroxy analog
AUTHOR(S): Phillips, G. J.; Citron, T. L.; Sage, J. S.; Cummins, K. A.; Cecava, M. J.; McNamara, J. P.
CORPORATE SOURCE: CH2M Hill, Hanford, WA, USA
SOURCE: Journal of Dairy Science (2003), 86(11), 3634-3647
CODEN: JDSCAE; ISSN: 0022-0302
PUBLISHER: American Dairy Science Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of prepartum dietary protein intake and dietary amino acid balance on milk production, adaptations in body fat, and blood serum protein and amino acid concns. (and indirectly body protein breakdown) in **early** lactation were studied in 42 multiparous Holstein dairy cows. The cows were fed diets containing 11 or 14% crude protein (CP) with or without 20 g methionine hydroxy analog daily for 21 days prepartum and then were fed common diet with 17% CP for 120 days postpartum, with or without 50 g methionine hydroxy analog (Rhodimet AT-88) daily. The dry matter (DM) intake postpartum averaged 25.4 kg and milk production 41.6 kg. Cows fed the 14% CP diet ate 0.7 kg more DM and gave 1.7 kg more milk than those fed the 11% CP diet prepartum. Cows fed the methionine hydroxy analog prepartum lost less body protein from -14 to +60 days in milk. From day 60 to 120, body fat increased 8.5 and 11.5 kg in low- and high-protein groups and body protein increased 0.5 and 1.0 kg. Blood serum concns. of branched-chain amino acids fell 17% in the first few weeks postpartum, lysine fell 15%, histidine fell 16%, methionine increased 20%, and cysteine increased 30%. The serum 3-methylhistidine/creatinine ratio was determined to indicate muscle protein degradation An increase in this ratio 7 days postpartum indicated increased body protein breakdown and there was no effect of prepartum ration composition Increased protein intake prepartum may allow more feed intake and milk production postpartum. Supplementing the methionine analog to a ration already balanced in methionine by contemporary models may spare body protein.

IT **583-91-5**
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(diets with differing amts. of protein and methionine hydroxy analog effects on adaptations in body muscle and fat in transition Holstein dairy cows)
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)

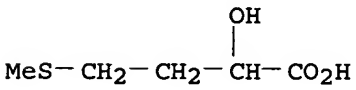


REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:590714 HCAPLUS
DOCUMENT NUMBER: 139:148557
TITLE: Protease **catalyzed** enantioselective oligomerization of α-hydroxy carboxylic acids and α-amino acids
INVENTOR(S): Lorbert, Stephen J.; Schasteen, Charles S.; Nam, Paul K.S.; Forciniti, Daniel; Rajesh, Mathur P.; Kapila, Shubhender
PATENT ASSIGNEE(S): Novus International, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 103 pp., Cont.-in-part of U.S. Ser. No. 699,946.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2003143661 | A1 | 20030731 | US 2002-136974 | | 20020502 |
| US 6605590 | B1 | 20030812 | US 2000-699946 | | 20001030 |
| US 2004048347 | A1 | 20040311 | US 2003-609825 | | 20030630 |
| PRIORITY APPLN. INFO.: | | | US 1999-162725P | P | 19991029 |
| | | | US 2000-699946 | A2 | 20001030 |
| | | | US 2001-288196P | P | 20010502 |

OTHER SOURCE(S): MARPAT 139:148557
AB An enzymic synthesis and composition of oligomers and co-oligomers comprised of α-hydroxy carboxylic acids and α-amino acids or peptides is disclosed. In a preferred embodiment, a α-hydroxy carboxylic acid with a specific chiral configuration is linked by an amide linkage to a α-amino acid specific with a specific chiral configuration or linked by an amide linkage to a peptide made up of α-amino acid monomers having identical chiral configurations. Proteolytic enzymes **catalyze** oligomerization of the α-hydroxy carboxylic acid and α-amino acid. The degree and distribution of oligomerization varies upon the type and concns. of different reaction mixts. utilized and upon the length of allowed reaction time. The resultant oligomers may be provided to animals such as ruminants as bioavailable amino acid supplements that are **resistant** to degradation in the rumen and other animals such as swine, poultry and aquatic animals.
IT **583-91-5D**, 2-Hydroxy-4-(methylthio)butyric acid, and derivs. of
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(protease **catalyzed** enantioselective oligomerization of α-hydroxy carboxylic acids and α-amino acids)
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



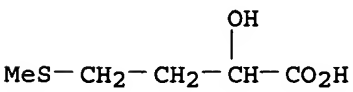
L33 ANSWER 5 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:428146 HCAPLUS
DOCUMENT NUMBER: 139:322807

TITLE: Effect of feeding methionine supplements with different rumen escape values on performance of high producing dairy cows in **early** lactation
AUTHOR(S): Uchida, K.; Mandebvu, P.; Ballard, C. S.; Sniffen, C. J.; Carter, M. P.
CORPORATE SOURCE: W.H. Miner Agricultural Research Institute, Chazy, NY, 12921-0090, USA
SOURCE: Animal Feed Science and Technology (2003), 107(1-4), 1-14
CODEN: AFSTDH; ISSN: 0377-8401
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A study was undertaken to compare a liquid form of methionine hydroxy analog (MHA; Novus Intl., Atlanta, GA, USA) and d,l-methionine, two methionine supplements with different rumen degradation escape values, on **early** lactational and reproductive performance by high producing dairy cows. Forty pregnant Holstein cows housed in a free-stall barn, were blocked by parity, date of calving, and previous 305-day mature equivalent milk production, and at calving were assigned randomly to one of two total mixed rations (TMR) containing MHA, or d,l-methionine, and group-fed for ad libitum intake. Cows spent 33±15.0 days in the fresh group, after which they were moved to the high producing group where they stayed up to 8-wk postpartum. The TMR were formulated to meet approx. 100% of required methionine, lysine, and other essential amino acids. An adequate amount of d,l-methionine was fed in order to provide a similar amount of methionine postruminally as provided by MHA, assuming a rumen degradation escape value of 40% for MHA and 22% for d,l-methionine. The TMR had forage to concentrate ratio of 40 to 60% for fresh group cows and 42 to 58% for high group cows. There were no differences between **treatments** in milk yield, content of milk fat, CP and true protein, linear somatic cell count, change in body condition score, and days to first service. In conclusion, d,l-methionine performed as well as MHA in promoting milk yield and contents of milk fat and protein when fed at levels aimed at supplying similar amts. of methionine postruminally as would be supplied by MHA fed at the recommended level.

IT **583-91-5**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (effect of feeding Met supplements with different rumen escape values on performance of high producing dairy cows in **early** lactation)

RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:537491 HCAPLUS
DOCUMENT NUMBER: 135:117260
TITLE: **Therapeutic** use of D-**methionine** to reduce the toxicity of **ototoxic** drugs, noise, and radiation

INVENTOR(S): Campbell, Kathleen C. M.
PATENT ASSIGNEE(S): Southern Illinois University School of Medicine, USA
SOURCE: U.S., 23 pp., Cont.-in-part of U.S. 6,187,817.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 6265386 | B1 | 20010724 | US 1998-57065 | 19980408 |
| US 6187817 | B1 | 20010213 | US 1997-942845 | 19971002 |
| PT 1019036 | T | 20031128 | PT 1998-915362 | 19980408 |
| ES 2202834 | T3 | 20040401 | ES 1998-915362 | 19980408 |
| US 2002019443 | A1 | 20020214 | US 2001-911195 | 20010723 |
| US 2004110719 | A1 | 20040610 | US 2003-694448 | 20031027 |
| US 2004127568 | A1 | 20040701 | US 2003-694432 | 20031027 |

PRIORITY APPLN. INFO.: US 1997-942845 A2 19971002
US 1996-27750P P 19961003
US 1998-57065 A2 19980408
US 2001-911195 A1 20010723

AB **Methods** of **preventing** or reducing **hearing** or balance loss, damage to **ear** cells, weight loss, gastrointestinal toxicity, neurotoxicity, alopecia, and prolonging survival in **patients** undergoing **treatment** with **therapeutically** effective amts. of **platinum**-containing **chemotherapeutic** agents such as cisplatin are provided. **Methods** are also provided for **preventing** or reducing such symptoms in **patients** undergoing **treatment** with loop diuretics, aminoglycoside antibiotics, iron chelating agents, quinine, and quinidine, or those who have been exposed to toxic levels of noise or radiation. These **methods** comprise administering an effective amount of a **methionine** protective agent, such as D-**methionine**, prior to, simultaneously with, or subsequently to administration of the **platinum**-containing **chemotherapeutic** agent, loop diuretic agent, etc., or exposure to noise or radiation. Combinations of these time periods can also be employed.

IT **7439-89-6**, Iron, biological studies
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chelating agents; **therapeutic** use of D-**methionine** and related compds. to reduce toxicity of **ototoxic** drugs, noise, **platinum**-containing antitumor drugs, and radiation)

RN 7439-89-6 HCAPLUS
CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

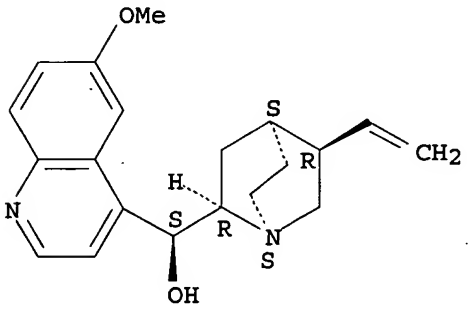
Fe

IT **56-54-2**, Quinidine **57-92-1**, Streptomycin, biological studies **59-01-8**, Kanamycin **114-07-8**, Erythromycin **130-95-0**, Quinine **1403-66-3**, Gentamicin **1404-04-2**, Neomycin **1404-90-6**, Vancomycin **6379-56-2**, Hygromycin **7542-37-2**, Paromomycin **14096-51-6**, Dichloro(ethylenediamine)**platinum**(II) **14215-58-8**, Chloro(diethylenetriamine)**platinum**(II) chloride **14913-33-8**, trans-**Diamminedichloroplatinum** (II) **15663-27-1**, Cisplatin **20115-64-4**

**32986-56-4**, Tobramycin **37517-28-5**, Amikacin
**41575-93-3** **41575-94-4**, Carboplatin **41666-77-7**
**56391-56-1**, Netilmicin **62928-11-4**, Iproplatin
**64363-09-3** **67254-31-3** **74790-08-2**, Spiroplatin
**114579-59-8** **141610-50-6** **148977-78-0**
**149055-58-3**
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**therapeutic** use of D-**methionine** and related compds. to reduce toxicity of **ototoxic** drugs, noise, **platinum**-containing antitumor drugs, and radiation)

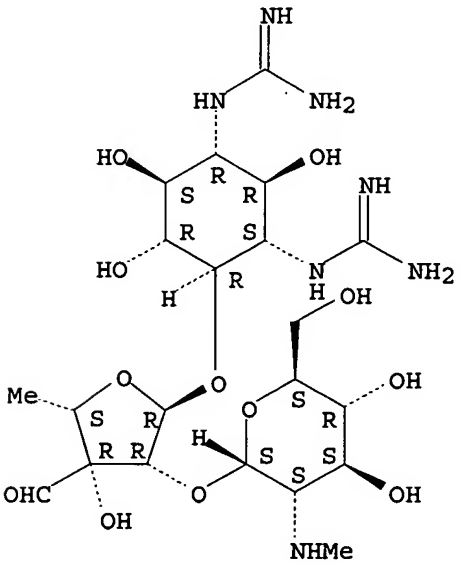
RN 56-54-2 HCAPLUS
CN Cinchonan-9-ol, 6'-methoxy-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




RN 57-92-1 HCAPLUS
CN D-Streptamine, O-2-deoxy-2-(methylamino)-α-L-glucopyranosyl-(1→2)-O-5-deoxy-3-C-formyl-α-L-lyxofuranosyl-(1→4)-N,N'-bis(aminoiminomethyl)- (9CI) (CA INDEX NAME)

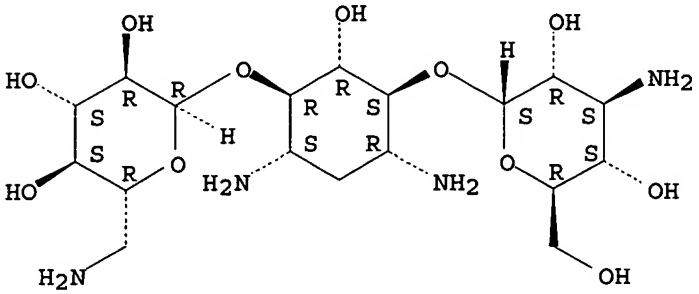
Absolute stereochemistry.




RN 59-01-8 HCAPLUS
CN D-Streptamine, O-3-amino-3-deoxy-α-D-glucopyranosyl-(1→6)-O-

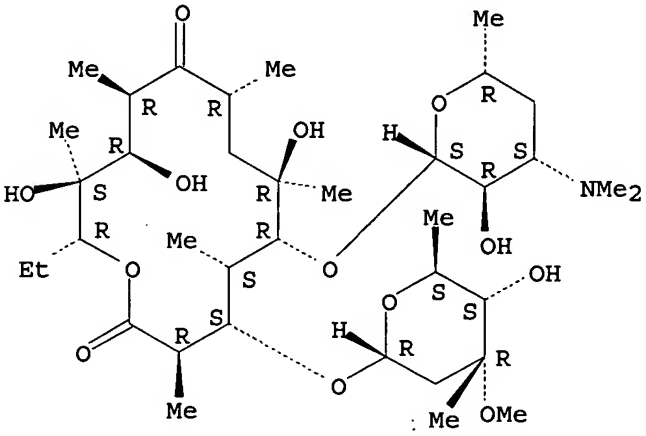
[6-amino-6-deoxy-α-D-glucopyranosyl-(1→4)]-2-deoxy- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



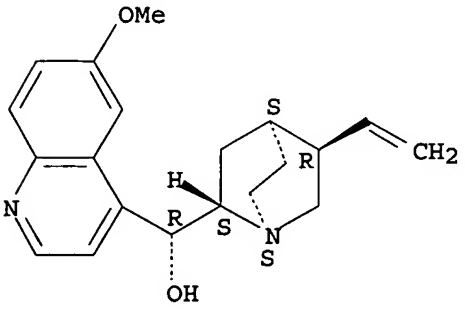
RN 114-07-8 HCAPLUS
CN Erythromycin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 130-95-0 HCAPLUS
CN Cinchonan-9-ol, 6'-methoxy-, (8α,9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



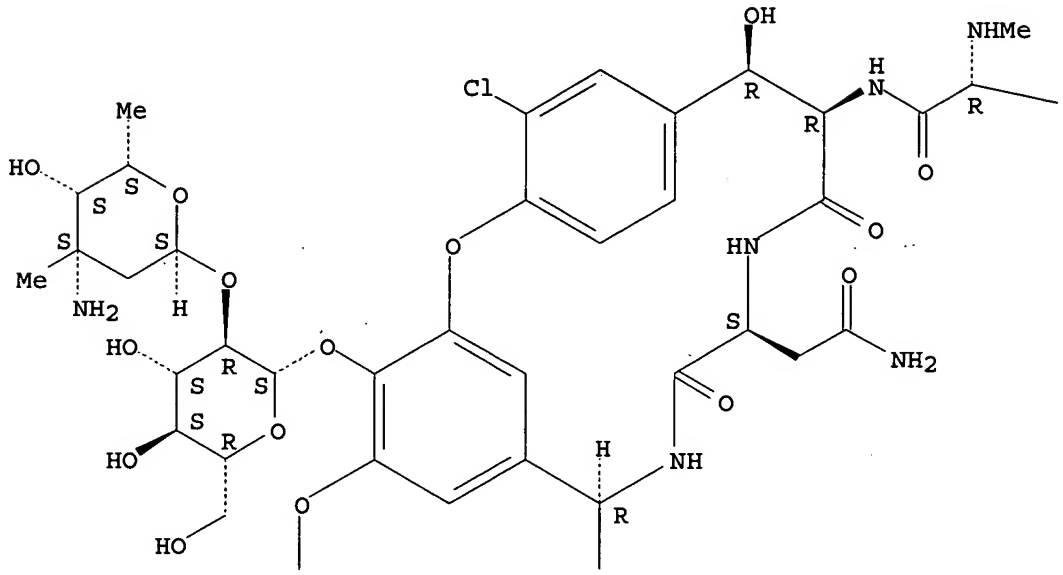
RN 1403-66-3 HCAPLUS
CN Gentamicin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 1404-04-2 HCAPLUS
CN Neomycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 1404-90-6 HCAPLUS
CN Vancomycin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

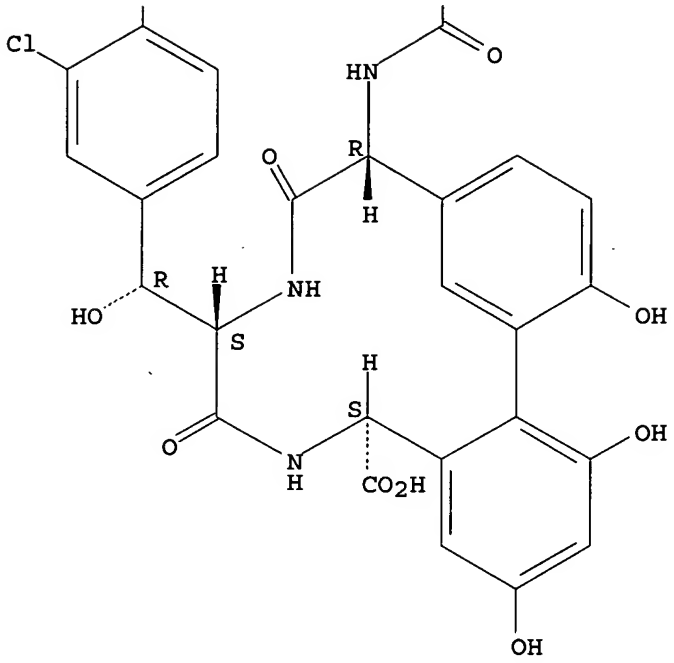
PAGE 1-A




PAGE 1-B

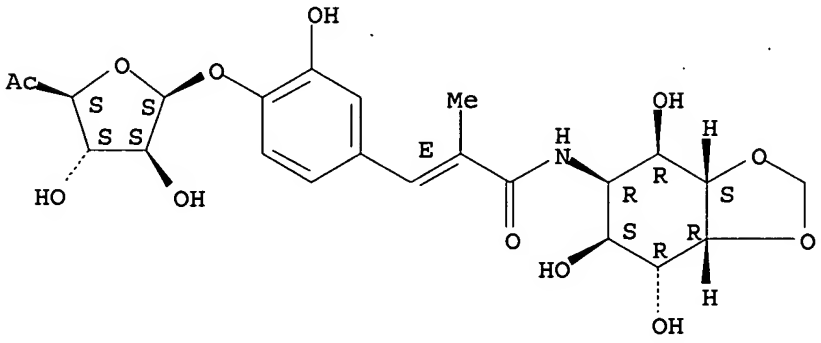
Bu-i

PAGE 2-A



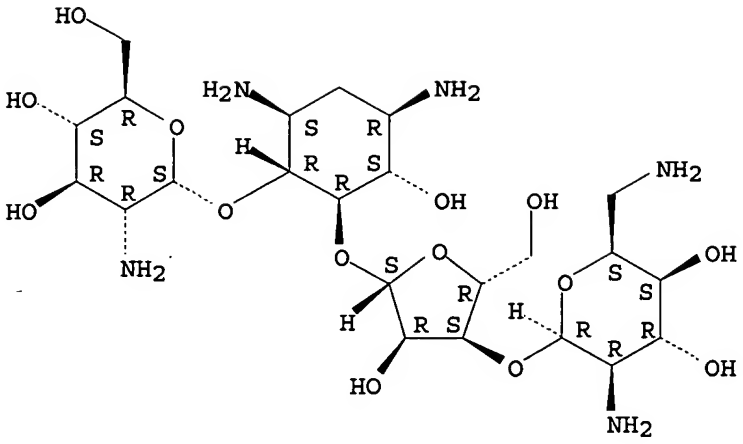
RN 6379-56-2 HCAPLUS
CN D-neo-Inositol, 5-deoxy-5-[[(2E)-3-[4-[(6-deoxy-β-D-arabino-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-propenyl]amino]-1,2-O-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

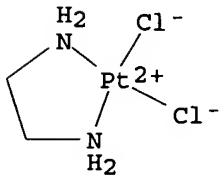


RN 7542-37-2 HCAPLUS
CN D-Streptamine, O-2-amino-2-deoxy-α-D-glucopyranosyl-(1→4)-O-[O-2,6-diamino-2,6-dideoxy-β-L-idopyranosyl-(1→3)-β-D-ribofuranosyl-(1→5)]-2-deoxy- (9CI) (CA INDEX NAME)

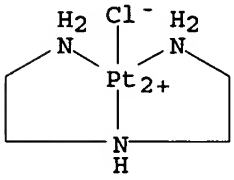
Absolute stereochemistry.



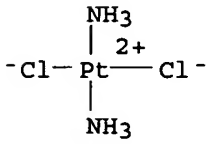
RN 14096-51-6 HCAPLUS
CN Platinum, dichloro(1,2-ethanediamine-κN,κN')-, (SP-4-2)- (9CI) (CA INDEX NAME)



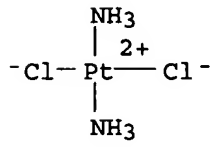
RN 14215-58-8 HCAPLUS
CN Platinum(1+), [N-[2-(amino-κN)ethyl]-1,2-ethanediamine-κN,κN']chloro-, chloride, (SP-4-2)- (9CI) (CA INDEX NAME)



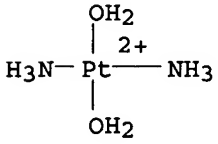
RN 14913-33-8 HCAPLUS
CN Platinum, diamminedichloro-, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 15663-27-1 HCAPLUS
CN Platinum, diamminedichloro-, (SP-4-2)- (9CI) (CA INDEX NAME)

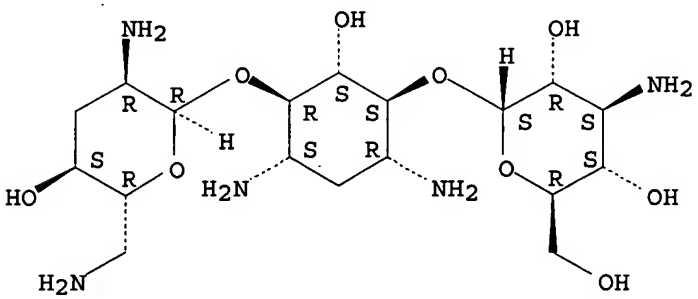


RN 20115-64-4 HCAPLUS
CN Platinum(2+), diamminediaqua-, (SP-4-2)- (9CI) (CA INDEX NAME)



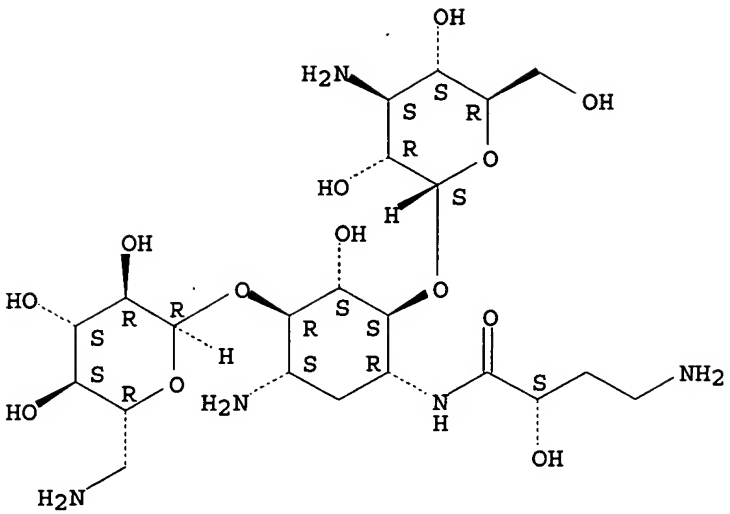
RN 32986-56-4 HCAPLUS
CN D-Streptamine, O-3-amino-3-deoxy-α-D-glucopyranosyl-(1→6)-O-[2,6-diamino-2,3,6-trideoxy-α-D-ribo-hexopyranosyl-(1→4)]-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

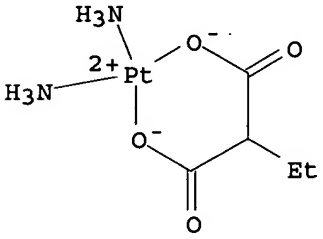


RN 37517-28-5 HCAPLUS
CN D-Streptamine, O-3-amino-3-deoxy-α-D-glucopyranosyl-(1→6)-O-[6-amino-6-deoxy-α-D-glucopyranosyl-(1→4)]-N1-[(2S)-4-amino-2-hydroxy-1-oxobutyl]-2-deoxy- (9CI) (CA INDEX NAME)

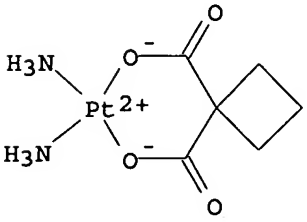
Absolute stereochemistry. Rotation (-).



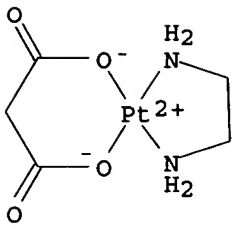
RN 41575-93-3 HCAPLUS
CN Platinum, diammine[ethylpropanedioato(2-)-κO1,κO3]-, (SP-4-2)-
(9CI) (CA INDEX NAME)



RN 41575-94-4 HCAPLUS
CN Platinum, diammine[1,1-cyclobutanedi(carboxylato-κO)(2-)]-,
(SP-4-2)- (9CI) (CA INDEX NAME)

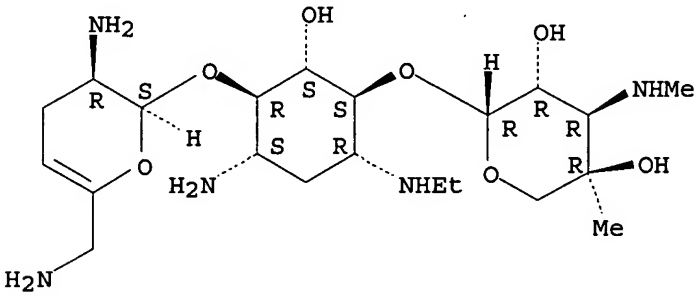


RN 41666-77-7 HCAPLUS
CN Platinum, (1,2-ethanediamine-κN,κN')[propanedioato(2-)-
κO1,κO3]-, (SP-4-2)- (9CI) (CA INDEX NAME)

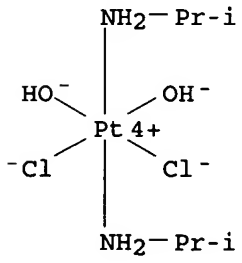


RN 56391-56-1 HCAPLUS
CN D-Streptamine, O-3-deoxy-4-C-methyl-3-(methylamino)-β-L-arabinopyranosyl-(1→6)-O-[2,6-diamino-2,3,4,6-tetradeoxy-α-D-glycero-hex-4-enopyranosyl-(1→4)]-2-deoxy-N1-ethyl- (9CI) (CA INDEX NAME)

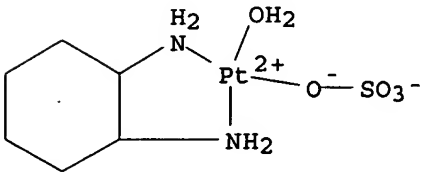
Absolute stereochemistry.



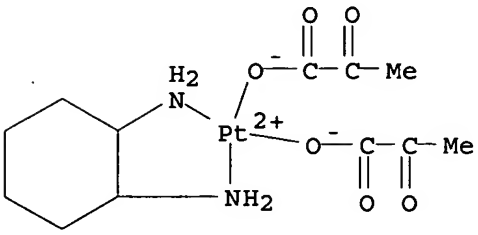
RN 62928-11-4 HCAPLUS
CN Platinum, dichlorodihydroxybis(2-propanamine)-, (OC-6-33)- (9CI) (CA INDEX NAME)



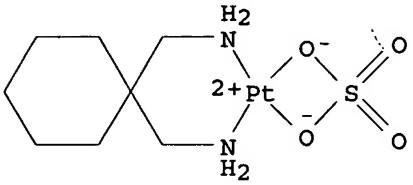
RN 64363-09-3 HCAPLUS
CN Platinum, aqua(1,2-cyclohexanediamine-κN,κN')[sulfato(2-)-κO]-, (SP-4-3)- (9CI) (CA INDEX NAME)



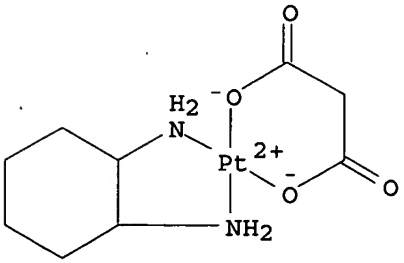
RN 67254-31-3 HCAPLUS
CN Platinum, (1,2-cyclohexanediamine-κN,κN')bis(2-oxopropanoato-κO)-, (SP-4-2)- (9CI) (CA INDEX NAME)



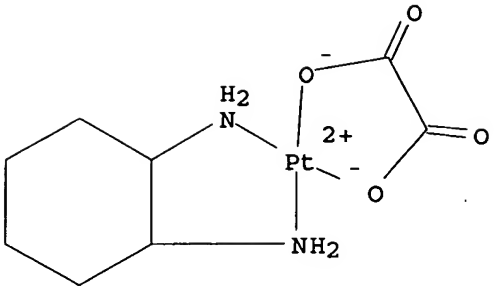
RN 74790-08-2 HCAPLUS
CN Platinum, (1,1-cyclohexanedimethanamine-κN,κN')[sulfato(2-)-κO,κO']-, (SP-4-2)- (9CI) (CA INDEX NAME)



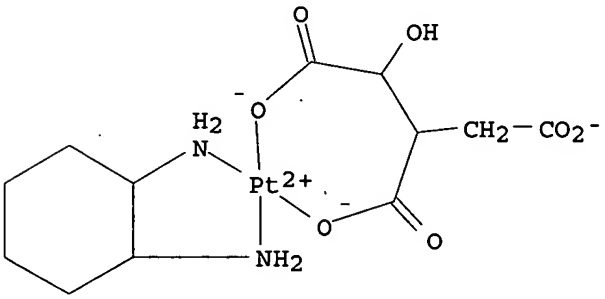
RN 114579-59-8 HCAPLUS
CN Platinum, (1,2-cyclohexanediamine-κN,κN')[propanedioato(2-)-κO1,κO3]-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 141610-50-6 HCAPLUS
CN Platinum, (1,2-cyclohexanediamine-κN,κN')[ethanedioato(2-)-κO1,κO2]-, (SP-4-2)- (9CI) (CA INDEX NAME)

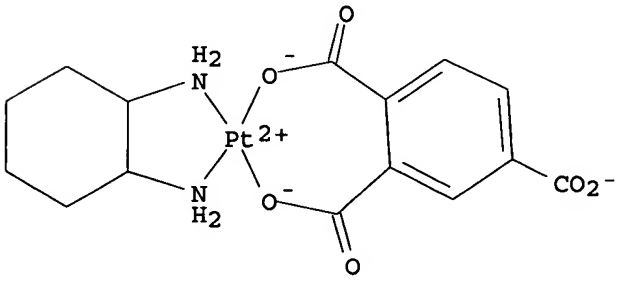


RN 148977-78-0 HCAPLUS
CN Platinate(1-), (1,2-cyclohexanediamine-κN,κN')[1-hydroxy-1,2,3-propanetricarboxylato(3-)-κO1,κO2]-, hydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)



● $H^+$

RN 149055-58-3 HCAPLUS
CN Platinate(1-), [1,2,4-benzenetricarboxylato(3-)-κO1,κO2](1,2-cyclohexanediamine-κN,κN')-, hydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)

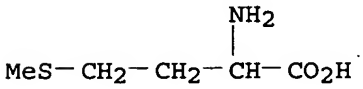


● $H^+$

IT **59-51-8, Methionine 63-68-3, L-Methionine**, biological studies **348-67-4, D-**

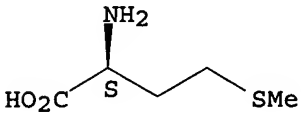
**Methionine 502-83-0**, Methioninol **1319-79-5**
**6094-76-4**, **Homomethionine 13073-35-3**,
Ethionine **29908-03-0**, **S-Adenosyl-L**
**-methionine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**therapeutic** use of D-**methionine** and related compds. to reduce toxicity of **ototoxic** drugs, noise, **platinum**-containing antitumor drugs, and radiation)

RN 59-51-8 HCAPLUS
CN Methionine (9CI) (CA INDEX NAME)



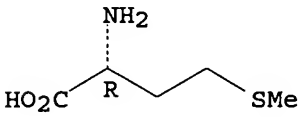
RN 63-68-3 HCAPLUS
CN L-Methionine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

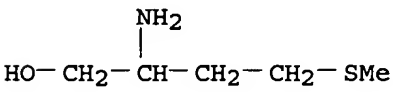


RN 348-67-4 HCAPLUS
CN D-Methionine (9CI) (CA INDEX NAME)

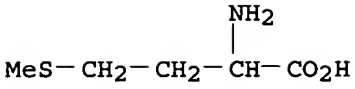
Absolute stereochemistry. Rotation (+).



RN 502-83-0 HCAPLUS
CN 1-Butanol, 2-amino-4-(methylthio)- (7CI, 8CI, 9CI) (CA INDEX NAME)

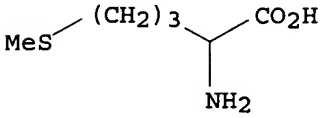


RN 1319-79-5 HCAPLUS
CN L-Methionine, hydroxy- (9CI) (CA INDEX NAME)



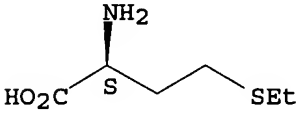
D1—OH

RN 6094-76-4 HCAPLUS
CN Norvaline, 5-(methylthio)- (9CI) (CA INDEX NAME)



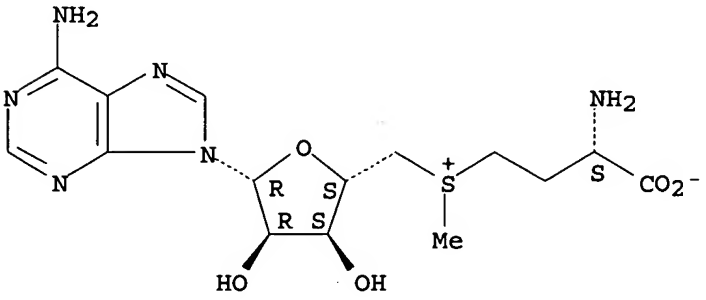
RN 13073-35-3 HCAPLUS
CN L-Homocysteine, S-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 29908-03-0 HCAPLUS
CN Adenosine, 5'-[[(3S)-3-amino-3-carboxypropyl]methylsulfonio]-5'-deoxy-, inner salt (9CI) (CA INDEX NAME)

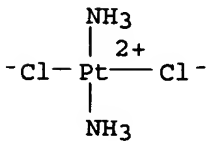
Absolute stereochemistry.



REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 7 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:474604 HCAPLUS
DOCUMENT NUMBER: 136:210154
TITLE: Round window membrane delivery of L-**methionine** provides protection from cisplatin **ototoxicity** without compromising **chemotherapeutic** efficacy

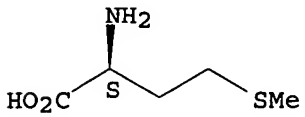
AUTHOR(S): Li, Geming; Frenz, Dorothy A.; Brahmblatt, Sapna; Feghali, Joseph G.; Ruben, Robert J.; Berggren, Diana; Arezzo, Joseph; Van De Water, Thomas R.
CORPORATE SOURCE: Department of Otolaryngology, Albert Einstein College of Medicine, Bronx, NY, USA
SOURCE: Neurotoxicology (2001), 22(2), 163-176
CODEN: NRTXDN; ISSN: 0161-813X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cisplatin (cis-**diamminedichloroplatinum**(II) (CDDP)) is a widely used, highly effective, oncolytic agent that has serious **ototoxic** side-effects. To test the effectiveness of local delivery of L-**methionine** (L-Met) as an otoprotective agent against CDDP **ototoxicity**, we used a rat model of a highly metastatic breast cancer tumor, i.e. Fisher 344 rats implanted with MTLn3 breast cancer cells. Four exptl. groups were evaluated - I: **untreated**; II: CDDP-**treated** (three dosages); III: systemically-delivered L-Met + CDDP-**treated**; IV: locally delivered L-Met + CDDP-**treated.** The integrity of the outer hair cells (OHCs) was determined using SEM; **hearing** was assessed by recording auditory brainstem responses (ABRs) at multiple frequencies. The **chemotherapeutic** effectiveness of CDDP was quantified by measuring changes in tumor mass and the presence of tumor metastasis. L-Met provided otoprotection of the OHCs against CDDP toxicity in the cochleae of rats following either systemic (III) or local (IV) administration. The ABRs were unchanged in each of the L-Met protection Groups (III and IV) and in the **untreated** animals of Group I. **Treatment** with CDDP only (II) induced significant **hearing** losses at both 16 and 18 kHz when compared to ABRs of **untreated** rats(I). CDDP was effective in **controlling** the MTLn3 initiated breast cancer tumors in the CDDP-**treated** (II) and the local L-Met protection, CDDP-**treated** (IV) Groups. In contrast, the tumors in the systemic L-Met protection, CDDP-**treated** Group (III) were not **controlled** by the CDDP **treatment** regime. This study demonstrates that local delivery of L-Met to the scala tympani of the cochlea via the round window membrane (IV) provides effective protection against CDDP **ototoxicity** without compromising its ability to **control** a highly metastatic form of cancer.
IT **15663-27-1**, Cisplatin
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(round window membrane delivery of L-**methionine** provides protection from cisplatin **ototoxicity** without compromising **chemotherapeutic** efficacy)
RN 15663-27-1 HCAPLUS
CN Platinum, diamminedichloro-, (SP-4-2)- (9CI) (CA INDEX NAME)



IT **63-68-3**, L-**Methionine**, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(round window membrane delivery of L-**methionine** provides

protection from cisplatin **ototoxicity** without compromising **chemotherapeutic** efficacy)
RN 63-68-3 HCAPLUS
CN L-Methionine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 8 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:338742 HCAPLUS
DOCUMENT NUMBER: 134:352782
TITLE: Oligomers and oligomeric segments of α-hydroxy carboxylic acids and α-amino acids and uses in improving bioavailability of nutrition supplement for ruminants
INVENTOR(S): Lorbert, Stephen J.; Schasteen, Charles S.; Nam, Paul K. S.; Forciniti, Daniel; Rajesh, Mathur P.; Kapila, Shubhender
PATENT ASSIGNEE(S): Novus International, Inc., USA
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

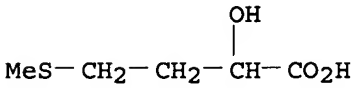
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001032906 | A2 | 20010510 | WO 2000-US29897 | 20001030 |
| WO 2001032906 | A3 | 20020214 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1224318 | A2 | 20020724 | EP 2000-976719 | 20001030 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |

PRIORITY APPLN. INFO.: US 1999-162725P P 19991029
WO 2000-US29897 W 20001030
OTHER SOURCE(S): MARPAT 134:352782
AB The invention is relates to the enzymic synthesis and composition of α-hydroxy carboxylic acid and α-amino acid or peptide co-oligomers wherein a residue of the α-hydroxy carboxylic acid is linked to a residue of the α-amino acid or peptide by an amide linkage. Proteolytic enzyme papain **catalyzes** co-oligomerization of the α-hydroxy carboxylic acid and α-amino acid. The degree and distribution of oligomerization varies upon the type and concns. of

different reaction mixts. utilized and upon the length of allowed reaction time. The present invention is further directed to a process for the preparation of an oligomer. The process comprises preparing a mixture containing (i) an enzyme, (ii) an α-hydroxycarboxylic acid and (iii) an α-amino acid or a peptide oligomer. The α-hydroxy carboxylic acid and the α-amino acid each are present in the mixture as a free acid, acid halide, amide, ester or anhydride independently of the other. The process further comprises forming an amide linkage between the residue of the α-hydroxy carboxylic acid and the residue of the α-amino acid or the peptide oligomer. The resultant oligomers may be provided to ruminants as bioavailable amino acid supplements that are **resistant** to degradation in the rumen.

IT **583-91-5**, 2-Hydroxy-4-(methylthio)butyric acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(oligomers and oligomeric segments of α-hydroxy carboxylic acids and α-amino acids and uses in improving bioavailability of nutrition supplement for ruminants)

RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:664545 HCAPLUS
DOCUMENT NUMBER: 134:55978
TITLE: Effects of DL-methionine hydroxyanalogue (MHA) or DL-methionine (DL-Met) on N-retention in broiler chickens and pigs. [Erratum to document cited in CA132:207304]
AUTHOR(S): Romer, Andrea; Abel, Hj.
CORPORATE SOURCE: Institut fur Tierphysiologie und Tierernahrung, Gottingen, 37077, Germany
SOURCE: Animal Feed Science and Technology (2000), 83(3-4), 325
CODEN: AFSTDH; ISSN: 0377-8401
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The reference to Walz and Pallauf (1996) was mistakenly cited in Section 4, page 301, line 9. The correct paragraph should read as follows: "As in broiler chickens there were also no differences in the effects of the two methionine sources on weight gain and feeding conversion ratios in pigs. This result confirms **earlier** studies (Chung and Baker, 1992; Reifsnyder et al., 1984), reporting equal effects of DL-Met and DL-MHA on growth performance in pigs.".

IT **583-91-5**, Alimet
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(dietary DL-methionine hydroxy analog and DL-methionine effects on N-retention in broiler chickens and pigs (Erratum))

RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)

L33 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:249071 HCAPLUS
DOCUMENT NUMBER: 130:262147
TITLE: Use of D-**methionine** or other **methionine** compound to reduce the toxicity of **ototoxic** drugs, noise, and radiation
INVENTOR(S): Campbell, Kathleen C. M.
PATENT ASSIGNEE(S): Southern Illinois University, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9917765 | A1 | 19990415 | WO 1998-US6960 | 19980408 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 6187817 | B1 | 20010213 | US 1997-942845 | 19971002 |
| CA 2303901 | AA | 19990415 | CA 1998-2303901 | 19980408 |
| AU 9869568 | A1 | 19990427 | AU 1998-69568 | 19980408 |
| AU 753039 | B2 | 20021003 | | |
| EP 1019036 | A1 | 20000719 | EP 1998-915362 | 19980408 |
| EP 1019036 | B1 | 20030625 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001518499 | T2 | 20011016 | JP 2000-514636 | 19980408 |
| AT 243511 | E | 20030715 | AT 1998-915362 | 19980408 |
| PT 1019036 | T | 20031128 | PT 1998-915362 | 19980408 |
| ES 2202834 | T3 | 20040401 | ES 1998-915362 | 19980408 |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 1997-942845 | A | 19971002 |
| | US 1996-27750P | P | 19961003 |
| | WO 1998-US6960 | W | 19980408 |

OTHER SOURCE(S): MARPAT 130:262147

AB **Methods** of **preventing** or reducing **hearing** or balance loss, damage to **ear** cells, weight loss, gastrointestinal toxicity, neurotoxicity, alopecia, and prolonging survival in **patients** undergoing **treatment** with **therapeutically** effective amts. of **platinum**-containing **chemotherapeutic** agents, e.g. cisplatin, are provided. **Methods** are also provided for **preventing** or reducing such symptoms in **patients** undergoing **treatment** with loop diuretics, aminoglycoside antibiotics, iron chelating agents, quinine, and quinidine, or those who have been exposed to toxic levels of noise or radiation. These **methods** comprise administering an

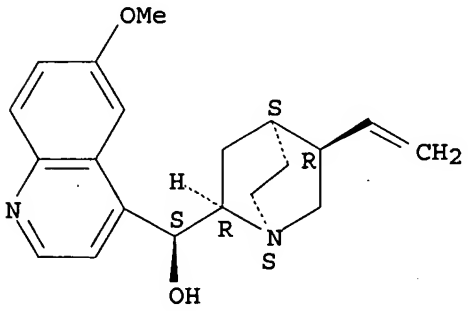
effective amount of a **methionine** protective agent, e.g. D-**methionine**, prior to, simultaneously with, or subsequently to administration of the **platinum**-containing **chemotherapeutic** agent, loop diuretic agent, etc., or exposure to noise or radiation. Combinations of these time periods can also be employed.

IT **7439-89-6**, Iron, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chelating agents; **methionine** compds. to reduce toxicity of **ototoxic** drugs, noise, and radiation)
RN 7439-89-6 HCAPLUS
CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

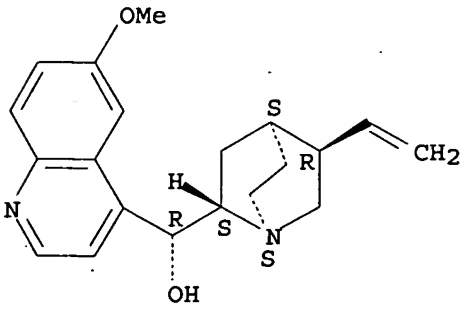
IT **56-54-2**, Quinidine **130-95-0**, Quinine **15663-27-1**, Cisplatin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**methionine** compds. to reduce toxicity of **ototoxic** drugs, noise, and radiation)
RN 56-54-2 HCAPLUS
CN Cinchonan-9-ol, 6'-methoxy-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

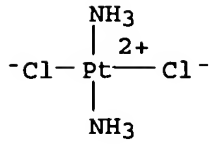



RN 130-95-0 HCAPLUS
CN Cinchonan-9-ol, 6'-methoxy-, (8α,9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

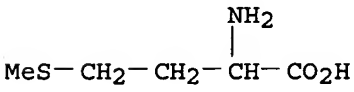



RN 15663-27-1 HCAPLUS
CN Platinum, diamminedichloro-, (SP-4-2)- (9CI) (CA INDEX NAME)

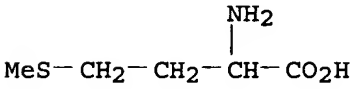


IT **59-51-8, Methionine 59-51-8D,**
**Methionine**, compds. **63-68-3, L-Methionine,**
biological studies **63-68-3D, L-Methionine**, derivs.,
biological studies **348-67-4, D-Methionine**
**348-67-4D, D-Methionine**, derivs. **502-83-0,**
Methioninol **1319-79-5 13073-35-3**, Ethionine
**29908-03-0, S-Adenosyl-L-**
**methionine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**methionine** compds. to reduce toxicity of **ototoxic** drugs, noise, and radiation)

RN 59-51-8 HCAPLUS
CN Methionine (9CI) (CA INDEX NAME)

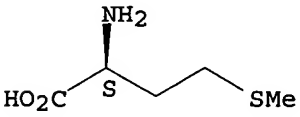


RN 59-51-8 HCAPLUS
CN Methionine (9CI) (CA INDEX NAME)



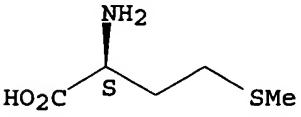
RN 63-68-3 HCAPLUS
CN L-Methionine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



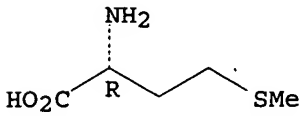
RN 63-68-3 HCAPLUS
CN L-Methionine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



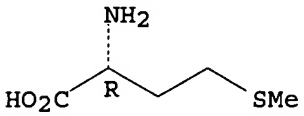
RN 348-67-4 HCAPLUS
CN D-Methionine (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

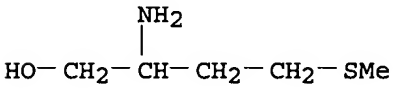


RN 348-67-4 HCAPLUS
CN D-Methionine (9CI) (CA INDEX NAME)

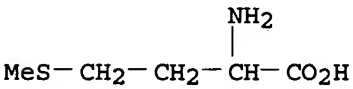
Absolute stereochemistry. Rotation (+).

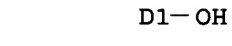


RN 502-83-0 HCAPLUS
CN 1-Butanol, 2-amino-4-(methylthio)- (7CI, 8CI, 9CI) (CA INDEX NAME)



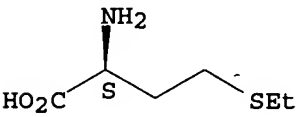
RN 1319-79-5 HCAPLUS
CN L-Methionine, hydroxy- (9CI) (CA INDEX NAME)





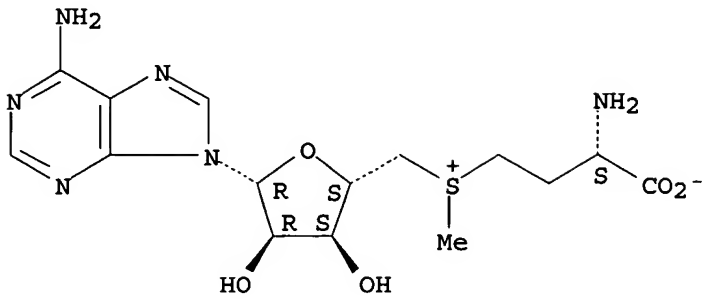
RN 13073-35-3 HCAPLUS
CN L-Homocysteine, S-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 29908-03-0 HCAPLUS
CN Adenosine, 5'-[[(3S)-3-amino-3-carboxypropyl]methylsulfonio]-5'-deoxy-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:219707 HCAPLUS
DOCUMENT NUMBER: 128:290226
TITLE: **Therapeutic** use of a **methionine** compound, such as D-**methionine**, to reduce the toxicity of **platinum**-containing antitumor compounds
INVENTOR(S): Campbell, Kathleen C. M.
PATENT ASSIGNEE(S): Southern Illinois University, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9814182 | A1 | 19980409 | WO 1997-US18114 | 19971002 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2265983 | AA | 19980409 | CA 1997-2265983 | 19971002 |
| CA 2265983 | C | 20031223 | | |
| AU 9748957 | A1 | 19980424 | AU 1997-48957 | 19971002 |
| AU 726392 | B2 | 20001109 | | |
| EP 930877 | A1 | 19990728 | EP 1997-911634 | 19971002 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001501626 | T2 | 20010206 | JP 1998-516973 | 19971002 |

PRIORITY APPLN. INFO.: US 1996-27750P P 19961003
WO 1997-US18114 W 19971002
OTHER SOURCE(S): MARPAT 128:290226
AB **Methods** are provided for **preventing** or reducing **hearing** or balance loss, damage to **ear** cells, weight loss, gastrointestinal toxicity, neurotoxicity, alopecia, and for prolonging survival in **patients** undergoing **treatment** with

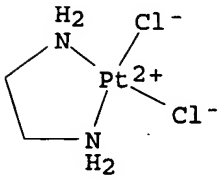
**therapeutically** effective amts. of **platinum**-containing **chemotherapeutic** agents, e.g. cisplatin, are provided. These **methods** comprise administering an effective amount of a **methionine** protective agent, e.g. D-**methionine**, prior to, simultaneously with, or subsequently to administration of the **platinum**-containing **chemotherapeutic** agent. Combinations of these time periods can also be employed.

IT **7440-06-4D**, **Platinum**, compds., biological studies
**14096-51-6**, Dichloro(ethylenediamine) **platinum** (II)
**14215-58-8 14913-33-8 15663-27-1**
**20115-64-4 38780-43-7 41575-93-3**
**41575-94-4 62928-11-4**, Iproplatin **64363-09-3**
**67254-31-3 74790-08-2**, Spiroplatin **88483-99-2**
**114579-59-8 141610-50-6 149055-58-3**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**methionine** compound for reduction of toxicity of **platinum** -containing antitumor compds.)

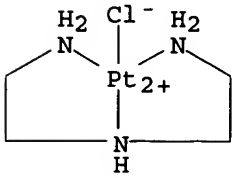
RN 7440-06-4 HCAPLUS
CN Platinum (8CI, 9CI) (CA INDEX NAME)

Pt

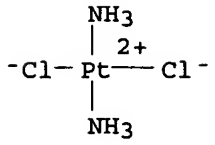
RN 14096-51-6 HCAPLUS
CN Platinum, dichloro(1,2-ethanediamine-κN,κN')-, (SP-4-2)- (9CI) (CA INDEX NAME)



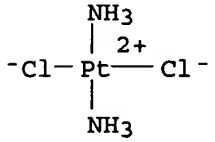
RN 14215-58-8 HCAPLUS
CN Platinum(1+), [N-[2-(amino-κN)ethyl]-1,2-ethanediamine-κN,κN']chloro-, chloride, (SP-4-2)- (9CI) (CA INDEX NAME)



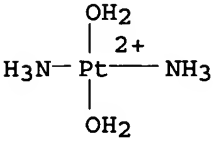
RN 14913-33-8 HCAPLUS
CN Platinum, diamminedichloro-, (SP-4-1)- (9CI) (CA INDEX NAME)



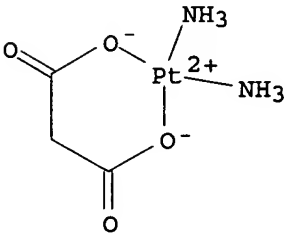
RN 15663-27-1 HCAPLUS
CN Platinum, diamminedichloro-, (SP-4-2)- (9CI) (CA INDEX NAME)



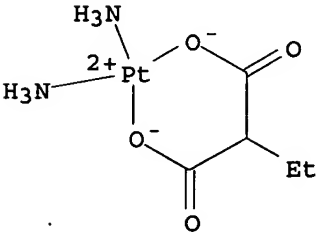
RN 20115-64-4 HCAPLUS
CN Platinum(2+), diammineddiaqua-, (SP-4-2)- (9CI) (CA INDEX NAME)



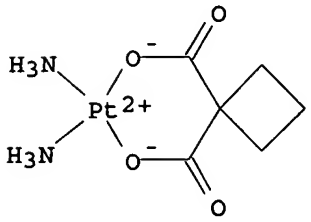
RN 38780-43-7 HCAPLUS
CN Platinum, diammine[propanedioato(2-)-κO1,κO3]-, (SP-4-2)-
(9CI) (CA INDEX NAME)



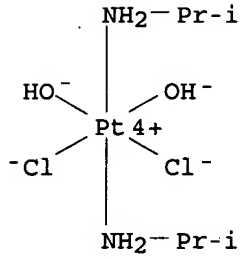
RN 41575-93-3 HCAPLUS
CN Platinum, diammine[ethylpropanedioato(2-)-κO1,κO3]-, (SP-4-2)-
(9CI) (CA INDEX NAME)



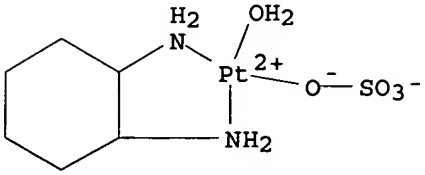
RN 41575-94-4 HCAPLUS
CN Platinum, diammine[1,1-cyclobutanedi(carboxylato-κO)(2-)]-, (SP-4-2)- (9CI) (CA INDEX NAME)



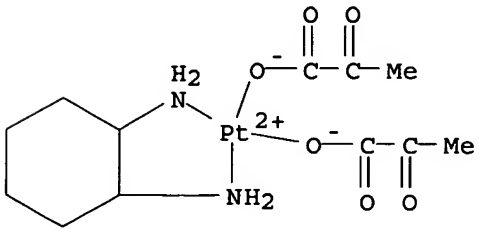
RN 62928-11-4 HCAPLUS
CN Platinum, dichlorodihydroxybis(2-propanamine)-, (OC-6-33)- (9CI) (CA INDEX NAME)



RN 64363-09-3 HCAPLUS
CN Platinum, aqua(1,2-cyclohexanediamine-κN,κN')[sulfato(2-)-κO]-, (SP-4-3)- (9CI) (CA INDEX NAME)

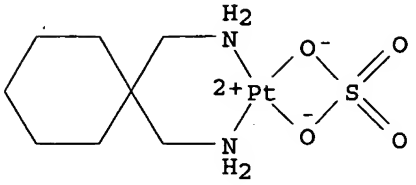


RN 67254-31-3 HCAPLUS
CN Platinum, (1,2-cyclohexanediamine-κN,κN')bis(2-oxopropanoato-κO)-, (SP-4-2)- (9CI) (CA INDEX NAME)

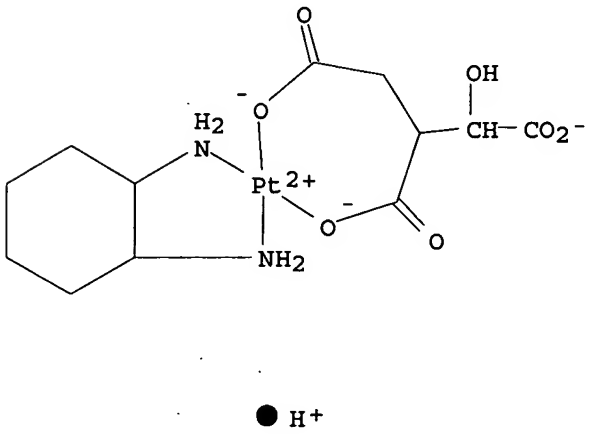


RN 74790-08-2 HCAPLUS

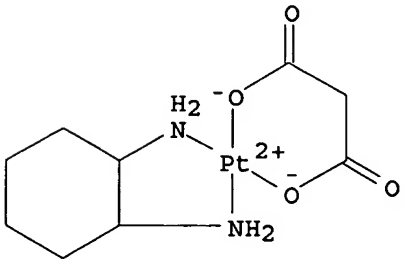
CN Platinum, (1,1-cyclohexanedimethanamine-κN,κN')[sulfato(2-)-κO,κO']-, (SP-4-2)- (9CI) (CA INDEX NAME)



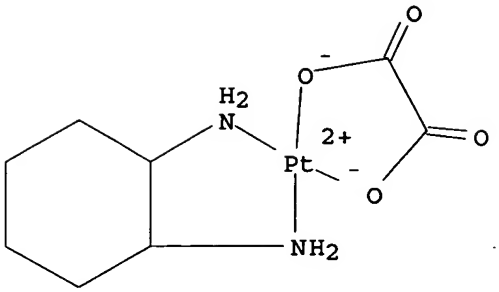
RN 88483-99-2 HCAPLUS
CN Platinate(1-), [3-(carboxy-κO)-2,3-dideoxypentarato(3-)-κO1](1,2-cyclohexanediamine-κN,κN')-, hydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)



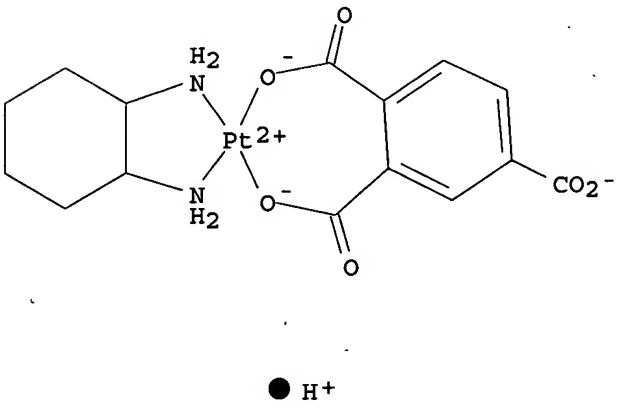
RN 114579-59-8 HCAPLUS
CN Platinum, (1,2-cyclohexanediamine-κN,κN')[propanedioato(2-)-κO1,κO3]-, (SP-4-2)- (9CI) (CA INDEX NAME)



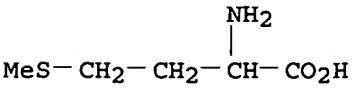
RN 141610-50-6 HCAPLUS
CN Platinum, (1,2-cyclohexanediamine-κN,κN')[ethanedioato(2-)-κO1,κO2]-, (SP-4-2)- (9CI) (CA INDEX NAME)



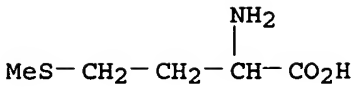
RN 149055-58-3 HCAPLUS
CN Platinate(1-), [1,2,4-benzenetricarboxylato(3-)-κO1,κO2](1,2-cyclohexanediamine-κN,κN')-, hydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)



IT **59-51-8**, **Methionine 59-51-8D**, **Methionine**, derivs. **63-68-3**, L-**Methionine**, biological studies **348-67-4**, D-**Methionine** **502-83-0**, Methioninol **1319-79-5 13073-35-3**, Ethionine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**methionine** compound for reduction of toxicity of **platinum** -containing antitumor compds.)
RN 59-51-8 HCAPLUS
CN Methionine (9CI) (CA INDEX NAME)

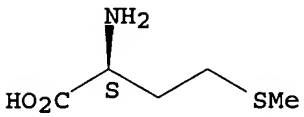


RN 59-51-8 HCAPLUS
CN Methionine (9CI) (CA INDEX NAME)



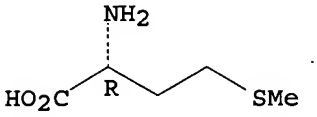
RN 63-68-3 HCAPLUS
CN L-Methionine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

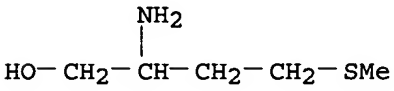


RN 348-67-4 HCAPLUS
CN D-Methionine (9CI) (CA INDEX NAME)

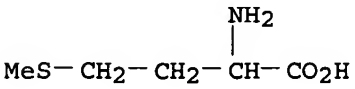
Absolute stereochemistry. Rotation (+).

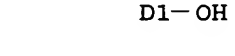


RN 502-83-0 HCAPLUS
CN 1-Butanol, 2-amino-4-(methylthio)- (7CI, 8CI, 9CI) (CA INDEX NAME)



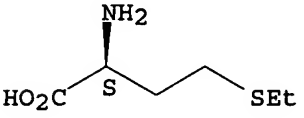
RN 1319-79-5 HCAPLUS
CN L-Methionine, hydroxy- (9CI) (CA INDEX NAME)





RN 13073-35-3 HCAPLUS
CN L-Homocysteine, S-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

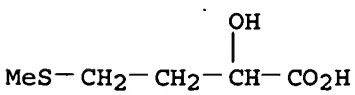


REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:177782 HCAPLUS
DOCUMENT NUMBER: 128:269942
TITLE: The relative effectiveness of 2-hydroxy-4-(methylthio)butanoic acid and DL-methionine in young swine
AUTHOR(S): Knight, C. D.; Atwell, C. A.; Wuelling, C. W.; Ivey, F. J.; Dibner, J. J.
CORPORATE SOURCE: Novus International, Inc., St. Charles, MO, 63304, USA
SOURCE: Journal of Animal Science (1998), 76(3), 781-787
CODEN: JANSAG; ISSN: 0021-8812
PUBLISHER: American Society of Animal Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We compared the nutritional effectiveness of 2-hydroxy-4-(methylthio)butanoic acid (HMB) and DL-methionine (DLM) as sources of L-methionine in methionine-deficient primary cultures of pig liver cells and methionine-deficient **early**-weaned pigs. Viable hepatocytes were obtained from minced pig liver and maintained in a high d., differentiated, non-proliferation cell culture system. The culture medium was supplemented with HMB, DLM, or L-methionine, and the cells were pulse-dosed with L-[U-14C]leucine for 24 h to determine the level of protein synthesis. Leucine incorporation per mg of protein indicated a 6-8-fold increase in protein synthesis with methionine levels 5-10 μM, regardless of the source of methionine. Two 24-pen replicate methionine dose titrns. were conducted with 95 **early**-weaned com. crossbred piglets. The pelleted corn, dried whey, and porcine blood plasma basal diet contained 1.5% lysine, 0.23% methionine, and 0.48% cystine, and was supplemented with 0, 0.05, or 0.10% methionine activity as DLM or HMB for 21 d. There was a 134, 104, and 61% increase in the cumulative average daily gain for each successive week of the study with a 30 and 19% improvement in the feed/gain ratio after 7 and 14 d. The growth performance due to the source of methionine did not differ and the slope ratio potency detns. (gain vs. intake of methionine source) of HMB vs. DLM indicated a 119, 111, and 95% relative activity for cumulative weekly performance. Thus, HMB and DLM may provide equimolar levels of methionine activity in swine.

IT **583-91-5**, Alimet
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(DL-methionine and 2-hydroxy-4-(methylthio)butanoic acid nutritional effectiveness in piglets)
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:589425 HCAPLUS
DOCUMENT NUMBER: 127:257225
TITLE: Stereoselective peripheral sensory neurotoxicity of

diaminocyclohexane **platinum** enantiomers related to ormaplatin and oxaliplatin

AUTHOR(S): Screnci, D.; Er, H. M.; Hambley, T. W.; Galettis, P.; Brouwer, W.; Mckeage, M. J.

CORPORATE SOURCE: Department of Pharmacology and Clinical Pharmacology, The University of Auckland School of Medicine, Auckland, N. Z.

SOURCE: British Journal of Cancer (1997), 76(4), 502-510
CODEN: BJCAAI; ISSN: 0007-0920

PUBLISHER: Churchill Livingstone

DOCUMENT TYPE: Journal

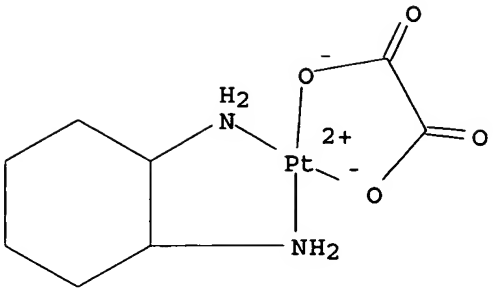
LANGUAGE: English

AB The diaminocyclohexane **platinum** (**Pt**(DACH)) derivs. ormaplatin and oxaliplatin have caused severe and dose-limiting peripheral sensory neurotoxicity in a clin. trial. We hypothesized that this toxicity could vary in relation to the biotransformation and stereochem. of these **Pt**(DACH) derivs. We prepared pure R,R and S,S enantiomers of ormaplatin (**Pt**(DACH)Cl4), oxaliplatin (**Pt**(DACH)oxalato) and their metabolites (**Pt**(DACH)Cl2 and **Pt**(DACH)**methionine**) and assessed their peripheral sensory neurotoxicity and tissue distribution in the rat and in vitro **anti-tumor** activity in **human** ovarian carcinoma cell lines. The R,R enantiomers of **Pt**(DACH)Cl4, **Pt**(DACH)oxalato and **Pt**(DACH)Cl2, induced peripheral sensory neurotoxicity at significantly lower cumulative doses (18 ± 5.7 vs 32±2.3 μmol kg-1; $P < 0.01$) and at **earlier** times (4 ± 1 vs 6.7±0.6 wk; P=0.016) during repeat-dose **treatment** than the S,S enantiomers. **Pt**(DACH)**methionine** enantiomers showed no biol. activity. There was no difference between **Pt**(DACH) enantiomers in the **platinum** concentration in sciatic nerve, dorsal root ganglia, spinal cord, brain or blood at the end of each experiment Three **human** ovarian carcinoma cell lines (41M, 41McisR and SKOV-3) showed no (or inconsistent) chiral discrimination in their sensitivity to **Pt**(DACH) enantiomers, whereas two cell lines (CH-1 and CH-1cisR) showed modest enantiomeric selectivity favoring the R,R isomer (more active). In conclusion, **Pt**(DACH) derivs. exhibit enantiomeric-selective peripheral sensory neurotoxicity during repeated dosing in rats favoring S,S isomers (less neurotoxic). They exhibited less chiral discrimination in their accumulation within peripheral nerves and in vitro **anti-tumor** activity.

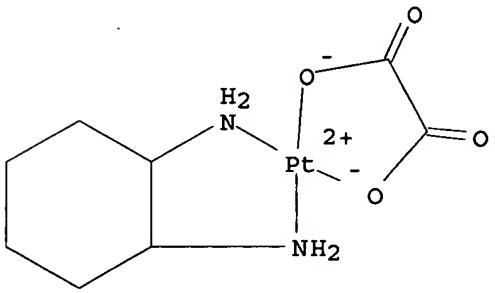
IT **61758-77-8 61825-94-3 61848-62-2 61848-66-6 96392-95-9 96392-96-0 195888-77-8 196108-97-1**
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(stereoselective peripheral sensory neurotoxicity of diaminocyclohexane **platinum** enantiomers related to ormaplatin and oxaliplatin)

RN 61758-77-8 HCAPLUS

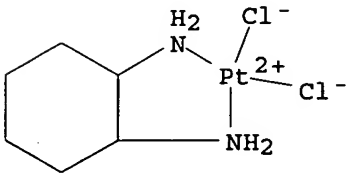
CN Platinum, [(1S,2S)-1,2-cyclohexanediamine-κN,κN'][ethanedioato(2-)-κO1,κO2]- (9CI) (CA INDEX NAME)



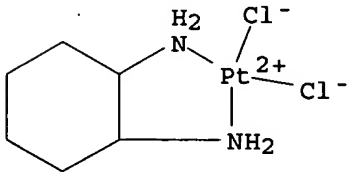
RN 61825-94-3 HCAPLUS
CN Platinum, [(1R,2R)-1,2-cyclohexanediamine-κN,κN'][ethanedioato (2-)-κO1,κO2]-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 61848-62-2 HCAPLUS
CN Platinum, dichloro[(1S,2S)-1,2-cyclohexanediamine-κN,κN']-, (SP-4-2)- (9CI) (CA INDEX NAME)

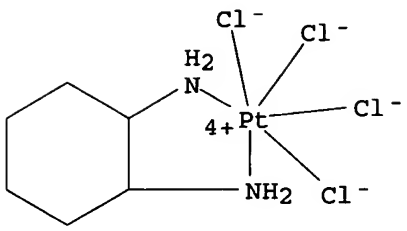


RN 61848-66-6 HCAPLUS
CN Platinum, dichloro[(1R,2R)-1,2-cyclohexanediamine-κN,κN']-, (SP-4-2)- (9CI) (CA INDEX NAME)

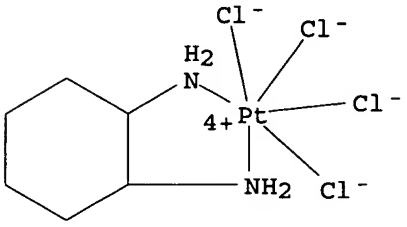


RN 96392-95-9 HCAPLUS
CN Platinum, tetrachloro[(1S,2S)-1,2-cyclohexanediamine-κN,κN']-,

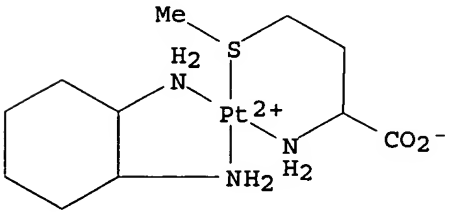
(OC-6-22)- (9CI) (CA INDEX NAME)



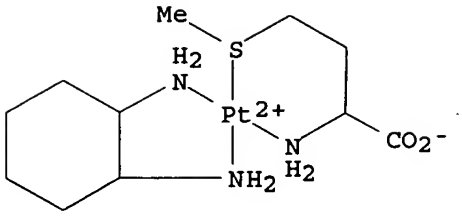
RN 96392-96-0 HCAPLUS
CN Platinum, tetrachloro[(1R,2R)-1,2-cyclohexanediamine-κN,κN']-, (OC-6-22)- (9CI) (CA INDEX NAME)



RN 195888-77-8 HCAPLUS
CN Platinum(1+), [(1R,2R)-1,2-cyclohexanediamine-κN,κN'](L-methioninato-κN,κS)-, monohydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 196108-97-1 HCAPLUS
CN Platinum(1+), (1,2-cyclohexanediamine-κN,κN')(L-methioninato-κN,κS)-, monohydrogen, [SP-4-3-(1S-trans)]- (9CI) (CA INDEX NAME)




● $H^+$

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:261094 HCAPLUS
DOCUMENT NUMBER: 126:311874
TITLE: **Treatment** with **inhibitors** of polyamine biosynthesis, which selectively lower intracellular spermine, does not affect the activity of alkylating agents but antagonizes the cytotoxicity of DNA topoisomerase II **inhibitors**
AUTHOR(S): Desiderio, M. A.; Bergamaschi, D.; Mascellani, E.; De Feudis, P.; Erba, E.; D'incalci, M.
CORPORATE SOURCE: Instituto di Patologia Generale, Universita degli Studi di Milano and Centro di studio sulla Patologia Cellulare, CNR, Milan, Italy
SOURCE: British Journal of Cancer (1997), 75(7), 1028-1034
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Inhibitors** of ornithine decarboxylase (ODC), such as α-difluoromethylornithine (DFMO), may influence the cytotoxicity of **anti-tumor** agents that interact with DNA. Intracellular levels of putrescine and spermidine were markedly reduced by ODC **inhibitors** while the level of spermine, which is the main polyamine in nuclei, was unchanged. By combining a novel **inhibitor** of ODC, such as (2R, 5R)-6-heptyne-2,5-diamine (MDL 72.175, MAP), with an **inhibitor** of S-**adenosylmethionine** decarboxylase (SAMDC), such as 5'-{[(Z)-4-aminobut-2-enyl]methylamino}-5'-deoxyadenosine (MDL 73.811, AbeAdo), spermine was selectively depleted in a **human** ovarian cancer cell line OVCAR-3 (i.e. spermine became almost undetectable whereas the levels of spermidine and putrescine were not affected). The depletion of spermine blocked DNA synthesis with a consequent accumulation of cells in the G1 phase of the cell cycle. **Pretreatment** with MAP plus AbeAdo did not change the cytotoxicity of alkylating agents, such as L-phenylalanine mustard (L-PAM), 1,4-bis (2'chloroethyl)-1, 4-diazabicyclo-[2.2.1] heptane diperchlorate (DABIS), 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU), cis-**diamminedichloroplatinum** (II) (cis-DDP), N-deformyl-N-[4-N-N,N-bis (2-chloroethylamino)benzoyl] (tallimustine) or CC-1065, whereas it markedly reduced the cytotoxicity of DNA topoisomerase II **inhibitors**, such as doxorubicin (DX) and 4'-demethylepipodophyllotoxin-5-(4,6-O)-ethylidene- β-D-glycopyranoside (VP-16). The addition of spermine before drug **treatment** restored

the sensitivity to the DNA topoisomerase II **inhibitors**, thus indicating that the reduced effect was related to the intracellular spermine level. The reason for the reduction in cytotoxicity is unclear, but it does not appear to be related to a cell cycle effect or to a decrease in the intracellular level of DNA topoisomerase II. Drugs that modify polyamine biosynthesis are under **early** clin. development as potential new **anti-tumor** agents. These findings illustrate the need for caution in combining such drugs with DNA topoisomerase II **inhibitors.**

IT **9024-60-6**, Ornithine decarboxylase **9036-20-8**, S-**Adenosylmethionine** decarboxylase **142805-56-9**, DNA topoisomerase II
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**inhibitors**; **treatment** with **inhibitors** of polyamine biosynthesis, which selectively lower intracellular spermine, does not affect the activity of alkylating agents but antagonizes the cytotoxicity of DNA topoisomerase II **inhibitors**)

RN 9024-60-6 HCAPLUS
CN Decarboxylase, ornithine (9CI) (CA INDEX NAME)

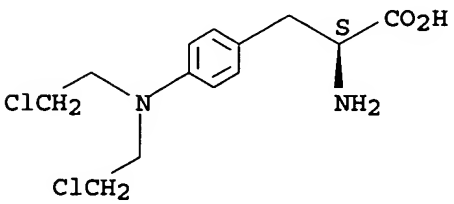
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9036-20-8 HCAPLUS
CN Decarboxylase, adenosylmethionine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 142805-56-9 HCAPLUS
CN Isomerase, deoxyribonucleate topo-, II (9CI) (CA INDEX NAME)

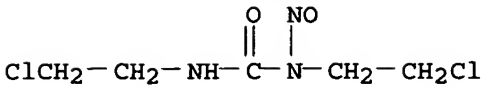
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **148-82-3**, L-Phenylalanine mustard **154-93-8**, BCNU **1020-94-6 15663-27-1 23214-92-8**, Doxorubicin **33419-42-0**, VP-16 **69866-21-3**, CC-1065 **88192-22-7**, MDL 72175 **115308-98-0**, Tallimustine **123642-27-3**, MDL 73811
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**treatment** with **inhibitors** of polyamine biosynthesis, which selectively lower intracellular spermine, does not affect the activity of alkylating agents but antagonizes the cytotoxicity of DNA topoisomerase II **inhibitors**)

RN 148-82-3 HCAPLUS
CN L-Phenylalanine, 4-[bis(2-chloroethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



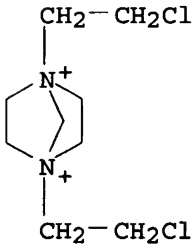

RN 154-93-8 HCAPLUS
CN Urea, N,N'-bis(2-chloroethyl)-N-nitroso- (9CI) (CA INDEX NAME)



RN 1020-94-6 HCAPLUS
CN 1,4-Diazoniabicyclo[2.2.1]heptane, 1,4-bis(2-chloroethyl)-, diperchlorate (8CI, 9CI) (CA INDEX NAME)

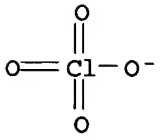
CM 1

CRN 21787-85-9
CMF C9 H18 Cl2 N2

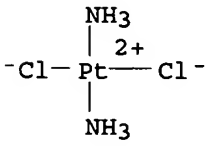


CM 2

CRN 14797-73-0
CMF Cl O4

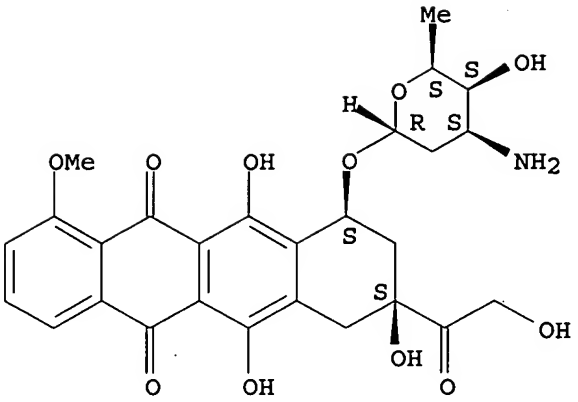


RN 15663-27-1 HCAPLUS
CN Platinum, diamminedichloro-, (SP-4-2)- (9CI) (CA INDEX NAME)



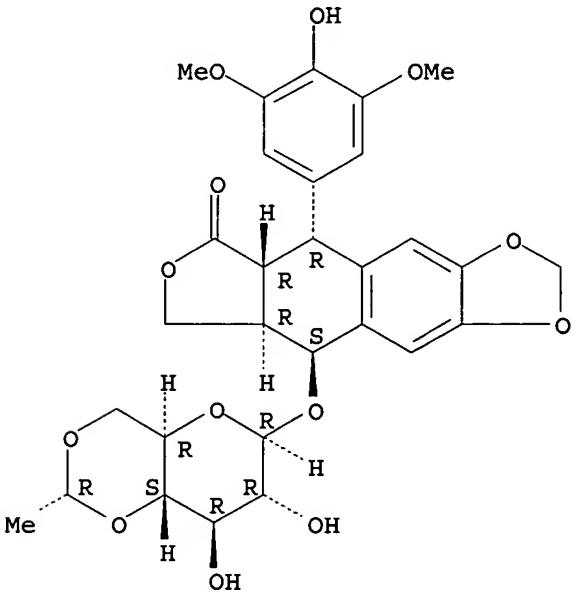
RN 23214-92-8 HCAPLUS
CN 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

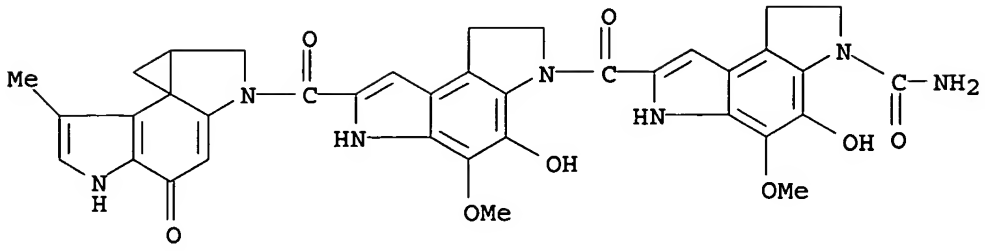


RN 33419-42-0 HCAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[[4,6-O-(1R)-ethylidene-β-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

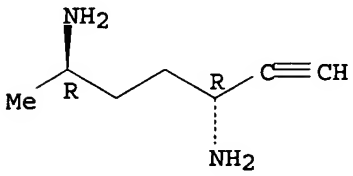


RN 69866-21-3 HCAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxamide, 7-[[1,6-dihydro-4-hydroxy-5-methoxy-7-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1,6-dihydro-4-hydroxy-5-methoxy-, (7bR,8aS)- (9CI) (CA INDEX NAME)



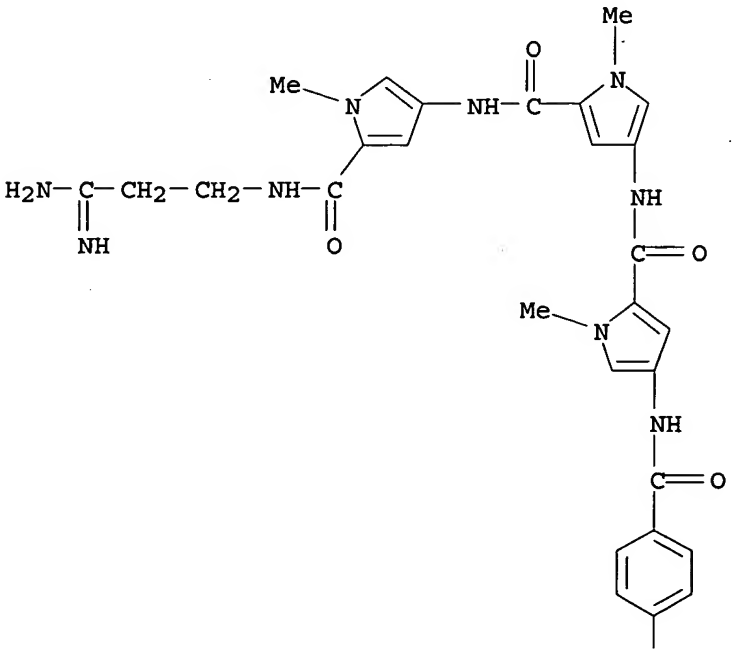
RN 88192-22-7 HCAPLUS
CN 6-Heptyne-2,5-diamine, (2R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

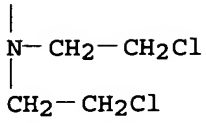


RN 115308-98-0 HCAPLUS
CN 1H-Pyrrole-2-carboxamide, N-[5-[[(3-amino-3-iminopropyl)amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[[4-[bis(2-chloroethyl)amino]benzoyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A

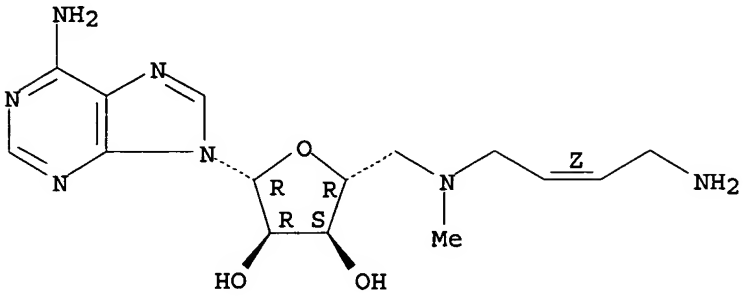


PAGE 2-A

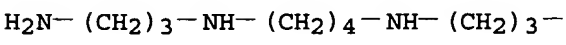


RN 123642-27-3 HCAPLUS
CN Adenosine, 5'-[[(2Z)-4-amino-2-butenyl]methylamino]-5'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **71-44-3**, Spermine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**treatment** with **inhibitors** of polyamine biosynthesis, which selectively lower intracellular spermine, does not affect the activity of alkylating agents but antagonizes the cytotoxicity of DNA topoisomerase II **inhibitors**)
RN 71-44-3 HCAPLUS
CN 1,4-Butanediamine, N,N'-bis(3-aminopropyl)- (8CI, 9CI) (CA INDEX NAME)

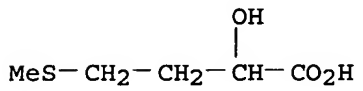


L33 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:655958 HCAPLUS
DOCUMENT NUMBER: 126:7060
TITLE: Studies on metabolism of broilers by using 14C-labeled DL-methionine and DL-methionine hydroxy analog Ca-salt
AUTHOR(S): Lingens, G.; Molnar, S.
CORPORATE SOURCE: Institute Animal Physiology Animal Nutrition, University Goettingen, Goettingen, D-37077, Germany
SOURCE: Archives of Animal Nutrition (1996), 49(2), 113-124
CODEN: AANUET
PUBLISHER: Harwood
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The incorporation of the growth-limiting DL-methionine (MET) into the body of 60-day-old male chickens was higher than that of the DL-methionine hydroxy analog (HM). Of the incorporated 14C, 17% was released in excrements and 15.8% in the expired air after MET feeding; and 4.4% was

released in excrements and 11.4% in the expired air after HM feeding. The incorporation of MET or HM in the digestive tract, blood, kidney, liver, gallbladder, lung, **heart**, spleen, and leg and breast muscles was also investigated.

IT **583-91-5**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(metabolism of broilers studied by 14C-labeled DL-methionine and DL-methionine hydroxy analog Ca-salt)

RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:494118 HCAPLUS
DOCUMENT NUMBER: 119:94118
TITLE: Fatty acid salt preparations containing other biologically active materials for use as feed supplements
INVENTOR(S): Vinci, Alfredo; Lajoie, M. Stephen; Sweeney, Thomas F.; Cummings, Kenneth R.
PATENT ASSIGNEE(S): Church and Dwight Co., Inc., USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9310669 | A1 | 19930610 | WO 1992-US7337 | 19920904 |
| W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG | | | | |
| AU 9225774 | A1 | 19930628 | AU 1992-25774 | 19920904 |
| EP 619706 | A1 | 19941019 | EP 1992-919798 | 19920904 |
| EP 619706 | B1 | 19991124 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE | | | | |
| BR 9206859 | A | 19960416 | BR 1992-6859 | 19920904 |
| AT 186817 | E | 19991215 | AT 1992-919798 | 19920904 |
| CA 2124925 | C | 20011002 | CA 1992-2124925 | 19920904 |
| US 5456927 | A | 19951010 | US 1993-149305 | 19931109 |
| WO 9512987 | A1 | 19950518 | WO 1994-US9137 | 19940822 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN | | | | |
| RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9476315 | A1 | 19950529 | AU 1994-76315 | 19940822 |
| PRIORITY APPLN. INFO.: | | | US 1991-802261 | A 19911204 |
| | | | US 1993-149305 | 19931109 |

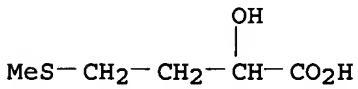
| | | |
|---|---|---|
| US 1993-7013 | | 19930121 |
| WO 1992-US7337 | A | 19920904 |
| WO 1994-US9137 | W | 19940822 |

AB The salts of C14-22 fatty acids for use as feed supplements for **cattle** are prepared with simultaneous incorporation of other feed supplements. By using the alkali **earth** metal salts of fatty acids, the fatty acids and the incorporated supplements have rumen bypass protection and so do not adversely affect rumen microflora. A series of feed supplements 35 were included in a stirred reaction mixture including palm oil fatty acids 700 , calcium oxide 100 and water 300 g. During the highly exothermic reaction nicotinic acid, methionine, lysine, or choline were broken down to a significant extent, but methionine hydroxy analog and nicotinamide were unaffected.

IT **583-91-5**
RL: BIOL (Biological study)
(as feed supplement, rumen bypass-protected, preparation of fatty acid calcium salts in relation to)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



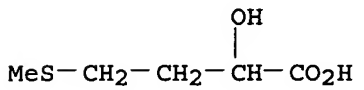
L33 ANSWER 17 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 1989:113544 HCAPLUS |
| DOCUMENT NUMBER: | 110:113544 |
| TITLE: | Effect of days of lactation and methionine hydroxy analog on incorporation of plasma fatty acids into plasma triglycerides |
| AUTHOR(S): | Pullen, David L.; Palmquist, D. L.; Emery, R. S. |
| CORPORATE SOURCE: | Dep. Anim. Sci., Michigan State Univ., East Lansing, MI, 48824, USA |
| SOURCE: | Journal of Dairy Science (1989), 72(1), 49-58 CODEN: JDSCAE; ISSN: 0022-0302 |
| DOCUMENT TYPE: | Journal |
| LANGUAGE: | English |

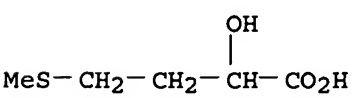
AB Cows were fed diets containing 0 or 30 g methionine hydroxy analog (I)/day starting 14 days prepartum. At .apprx.30 and 60 days postpartum, cows were continuously infused i.v. with 1-[14C]palmitic acid for 160 min to achieve steady-state labeling of plasma fatty acids and triglycerides. Turnover of fatty acids and transfer quotients for triglycerides and CO2 were 3.3 and 2.7 mmol/min; 13.0 and 10.0%; and 8.0 and 5.0%, for **control** and I, resp. Proportion of fatty acid turnover incorporated into triglycerides and CO2 were 14.0 and 15.0%; and 21.0 and 18.0, resp., for **control** and I. I increased 14C recovered in milk fat (52 vs. 36%). Plasma concentration of fatty acids, percent oxidized to CO2, and percent of CO2 from fatty acids decreased with increasing lactation days. Milk fat percent and yield, fatty acid turnover, and oxidation were pos. correlated with concentration of plasma fatty acids, whereas fatty acid incorporated into plasma triglyceride was neg. correlated with fatty acid concentration Apparently, hepatic triglyceride secretion is not increased in **early** lactation; further, no effects of analog on lipid metabolism were detected.

IT **583-91-5**, Methionine hydroxy analog

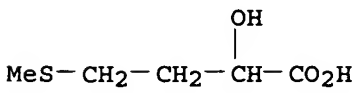
RL: BIOL (Biological study)
(fatty acid metabolism and triglyceride formation by dairy cows in lactation response to, feeding experiment in relation to)
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:438442 HCAPLUS
DOCUMENT NUMBER: 107:38442
TITLE: Effect of fasting and of methionine deficiency on L-methionine, DL-methionine and DL-2-hydroxy-4-methylthiobutanoic acid metabolism in broiler chicks
AUTHOR(S): Saunderson, C. Linda
CORPORATE SOURCE: Inst. Grassland Anim. Prod., AFRC, Roslin/Midlothian, EH25 9PS, UK
SOURCE: British Journal of Nutrition (1987), 57(3), 429-37
CODEN: BJNUAV; ISSN: 0007-1145
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Metabolism of L-[1-14C]methionine, DL-[1-14C]methionine, and DL-[1-14C]2-hydroxy-4-methylthiobutanoic acid (DL-HMB) by broiler chicks which had been fasted overnight or given a methionine-deficient diet was compared with fed (**control**) birds. The excretion of 14C-labeled material, total 14CO2 exhaled, 14C incorporation into tissue proteins, and the 14C-labeled material in HClO4-soluble tissue fractions were measured 6 h after injection of the 14C-labeled materials. The incorporation of 14C into tissue proteins and the relative rates of conversion of D-methionine and DL-HMB to L-methionine in tissues under different nutritional regimens were compared using protein-bound 14C:protein-free 14C values. Fasted birds exhaled more 14CO2 than **control** birds but excreted less 14C, while methionine-deficient birds behaved very similarly to the **control** animals in these respects. Fasted birds incorporated much less 14C into proteins of tissues other than liver and kidney from all 3 labeled tracers. The values for protein-bound 14C:protein-free 14C were lower in all tissues. Methionine-deficient birds had similar levels of 14C in tissue proteins but lower values for protein bound 14C:protein-free 14C. Examination of the values for protein-bound 14C:protein-free 14C suggest that brain and probably liver tissues from fasted and methionine-deficient birds showed improved rates of conversion of D-methionine and DL-HMB to L-methionine compared with **control** animals.
IT **583-91-5**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, by broiler chicks, fasting and methionine deficiency effect on)
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)

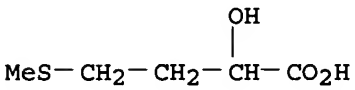


L33 ANSWER 19 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:144867 HCAPLUS
DOCUMENT NUMBER: 104:144867
TITLE: The occurrence of 4-methylthio-2-hydroxybutyrate in **human** urine
AUTHOR(S): Maartensson, Johannes
CORPORATE SOURCE: Dep. Clin. Chem., Univ. Hosp. Linkoeping, Linkoeping, S-581 85, Swed.
SOURCE: Analytical Biochemistry (1986), 154(1), 43-9
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A **method** for determination of 4-methylthio-2-hydroxybutyrate and 4-methylthio-2-oxobutyrate in **human** urine was devised, based on methoxime formation of the keto acid and a clean-up procedure using the strong anion-exchange resin AG 2X8 and EtOAc extraction After alkylation, the compds. were quantified by gas chromatog. using a flame photometric S-selective detector. Separation was done on a silanized glass column (6 ft) filled with 3% OV17 on Chromosorb WHP (100-200 mesh), with temps. of 220, 140, and 250° for injector, column, and detector, resp. The carrier gas was He. A normal urinary excretion of 0.14-0.25 mmol/mol creatinine and 0.07-0.22 mmol/mol creatinine of the α-hydroxy and α-keto acid, resp., was found, whereas a markedly elevated excretion of the hydroxy acid was noted in subjects with hypermethioninemia. The enzymic reduction of 4-methylthio-2-oxobutyric acid by lactate dehydrogenase:NAD+ oxidoreductase (EC 1.1.1.17) was also studied. The Km and Kequil values for 4-methylthio-2-oxobutyrate were 1.41 mM and 0.92 + 108 M-1. The Vmax value of the enzyme at infinite concns. of the 2 substrates was 7.2 μmol/s/μmol enzyme, which indicates low affinity and reduced **catalytic** activity compared to other known substrates of lactate dehydrogenase. The reaction product 4-methylthio-2-hydroxybutryrate was not **inhibitory** on the reaction. The M4 isoenzyme of lactate dehydrogenase (rabbit and pig muscle) had .apprx.20% of the activity of the H4 isoenzyme (pig **heart**) for the substrate.
IT **583-91-5P**
RL: ANT (Analyte); BPN (Biosynthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)
(determination of, in **human** urine by gas chromatog. in **health** and hypermethioninemia)
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 20 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:3567 HCAPLUS
DOCUMENT NUMBER: 104:3567
TITLE: Comparative metabolism of L-methionine, DL-methionine and DL-2-hydroxy-4-methylthiobutanoic acid by broiler chicks
AUTHOR(S): Saunderson, C. Linda
CORPORATE SOURCE: Poult. Res. Cent., Agric. Food Res. Counc., Roslin,

EH25 9PS, UK
SOURCE: British Journal of Nutrition (1985), 54(3), 621-33
CODEN: BJNUAV; ISSN: 0007-1145
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Metabolism, in broiler chicks, of DL-2-hydroxy-4-methylthiobutanoic acid (DL-HMB), DL-methionine and L-methionine was compared in vivo using 14C-labeled tracers. The distribution of L-[1-14C]methionine and DL-[1-14C]HMB in the major body tissues was examined for 120 min after administration. The relative oxidation (14CO2 exhaled), excretion, and incorporation into tissue protein of L-[1-14C]methionine, DL-[1-14C]methionine and DL-[1-14C]HMB were measured in fed birds. Tissue distribution of L-[1-14C]methionine and DL-[1-14C]HMB differed during 60-90 min following administration. The production of 14CO2 from each of the tracers was similar, but excretion of 14C-labeled material was very different with the greatest excretion from DL-[1-14C]HMB and the least from L-[1-14C]methionine. The incorporation of 14C into tissue proteins varied with the tracer given and the tissue examined Liver and kidney had equivalent incorporation from each of the tracers, whereas other tissues examined showed lower incorporation from DL-[1-14C]methionine and DL-[1-14C]HMB. Thus, DL-HMB, D-methionine, and L-methionine are metabolized differently in vivo and they are excreted in differing proportions. There is also a difference in the ability of each to act as a precursor for protein synthesis in tissues other than liver.
IT **583-91-5**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, by chicken)
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)

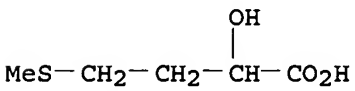


L33 ANSWER 21 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:217690 HCAPLUS
DOCUMENT NUMBER: 102:217690
TITLE: Studies of metabolites in **diarrheal** stool specimens containing Shigella species by frequency-pulsed electron capture gas-liquid chromatography
AUTHOR(S): Brooks, J. B.; Basta, M. T.; El Kholy, A. M.
CORPORATE SOURCE: Div. Bacterial Dis., Cent. Infect. Dis., Atlanta, GA, 30333, USA
SOURCE: Journal of Clinical Microbiology (1985), 21(4), 599-606
CODEN: JCMIDW; ISSN: 0095-1137
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Diarrheal** stool specimens and **control** stool specimens from Cairo, Egypt, were studied by frequency-pulsed electron capture gas chromatog. (FPEC-GLC). Cases involving S. sonnei, cases involving S. boydii, and cases involving S. flexneri were studied. The aqueous stools were centrifuged, extracted with organic solvents, and derivatized to form specific electron-capturing derivs. of carboxylic acids, alcs., hydroxy acids, and amines. Analyses were performed on high-resolution glass columns with an

instrument equipped with an extremely sensitive electron capture detector that is specific for the detection of electron-capturing compds. The **diarrheal** stools studied had specific FPEC-GLC profiles and contained metabolic markers that readily distinguished between the Shigella species studied and Escherichia coli producing heat-stable or heat-labile enterotoxins. S. sonnei Stools contained hexanoic acid, 2-hydroxy-4-methylmethiobutyric acid, and some unidentified alcs. that distinguished this organism from other enteric pathogens. S. boydii Produced an acid that was unique for this species, and S. flexneri produced alcs. that could be used to distinguish between it and other enteric organisms. The FPEC-GLC profiles obtained during this study were also very different from those reported **earlier** for Clostridium difficile and rotavirus. This study presents further evidence that the selectivity and sensitivity of FPEC-GLC **techniques** can be used to rapidly identify causative agents of diarrhea and detect phsiol. changes that occur in the gut during the course of **diarrheal** illness.

IT **583-91-5**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in feces of **humans** in diarrhea by gas chromatog.)

RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



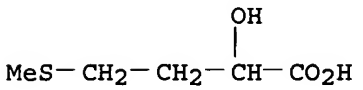
L33 ANSWER 22 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:478882 HCAPLUS
DOCUMENT NUMBER: 95:78882
TITLE: Influence of ration composition and energy balance on blood β-hydroxybutyrate (ketone) and plasma glucose concentrations of dairy cows in **early** lactation
AUTHOR(S): Herdt, T. H.; Stevens, J. B.; Linn, J.; Larson, V.
CORPORATE SOURCE: Dep. Large Anim. Clin. Sci., Univ. Minnesota, St. Paul, MN, 55108, USA
SOURCE: American Journal of Veterinary Research (1981), 42(7), 1177-80
CODEN: AJVRAH; ISSN: 0002-9645
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of ratio composition, with respect to concentrate, crude protein, and methionine hydroxy analog [**583-91-5**] content, on blood β-hydroxybutyrate [300-85-6] and plasma glucose [50-99-7] concns. was assessed in Holstein cows every 2 wk over the first 6 wk of lactation. The correlation of these metabolites with estimated energy balance, and the effects of these ration variables on this correlation were studied. High concentrate diets (60% of dry matter) compared with low concentrate diets (40% of dry matter) increased mean plasma glucose values and reduced mean blood β-hydroxybutyrate concentration Variation in crude protein and methionine hydroxy analog supplementation did not affect metabolite concentration The correlations between blood β-hydroxybutyrate and energy balance and between plasma glucose and energy balance were weak and subject to the influence of variation in ration composition Plasma glucose and blood

β-hydroxybutyrate concns. cannot be used as valid indicators of energy balance. However, it did appear that blood β-hydroxybutyrate might be used as an indicator of the relative glucogenic potential of dairy rations and that blood concns. of this metabolite could potentially be used to adjust factors in the ration which influence glucose availability to the cow.

IT **583-91-5**
RL: BIOL (Biological study)
(blood β-hydroxybutyrate and plasma glucose of dairy cows in relation to dietary)

RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)

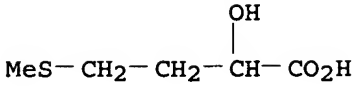


L33 ANSWER 23 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1978:103738 HCAPLUS
DOCUMENT NUMBER: 88:103738
TITLE: The use of whole barley diets fortified with solutions of urea, minerals and vitamins for lambs
AUTHOR(S): Oerskov, E. R.; Grubb, D. A.
CORPORATE SOURCE: Rowett Res. Inst., Bucksburn/Aberdeen, UK
SOURCE: Animal Feed Science and Technology (1977), 2(4), 307-14
CODEN: AFSTDH; ISSN: 0377-8401
DOCUMENT TYPE: Journal
LANGUAGE: English

AB For 1 experiment 45 **early**-weaned lambs were given one of the following 5 diets from weaning to slaughter: (1) whole barley with urea [57-13-6], minerals, and vitamins added as a concentrated solution; (2) as diet (1) plus 4 g/kg of Na2SO4 in solution; (3) as diet (2) plus 1.2 g of methionine hydroxy analog (MHA) [**583-91-5**]/kg; (4) as diet (2) plus 2.5 mL of 40% CH2O added per kg; (5) a **control** diet containing whole barley and 100 g/kg of a pelleted supplement based on fish meal. Growth rates (g/day) for the 5 **treatments** were 218,253,253,256, and 292. Addition of SO42- significantly increased growth rate and food utilization while MHA had no effect; formalin **treatment** reduced digestibility and food utilization. In a 2nd experiment 58 lambs were used to study the effect of protein supplements for lambs weaned at various ages and wts. Diets similar to (2) and (5) from experiment (1) were used, while an intermediate diet (6) was made from an equal mixture of diets (2) and (5). As weaning age increased and as live weight at weaning increased, the difference in growth rate and food utilization between lambs receiving diet (2) and those receiving diets (5) and (6) decreased. It is suggested that for most sheep production systems in which concs. are used either as the sole feed or as supplements, simple fortification of whole grain with the necessary nutrients is all that is required to achieve optimum results.

IT **583-91-5**
RL: BIOL (Biological study)
(feed experiment with, on lambs, barley in relation to)

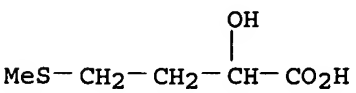
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 24 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1978:5165 HCAPLUS
DOCUMENT NUMBER: 88:5165
TITLE: Methionine hydroxy analog in diets for lactating cows
AUTHOR(S): Bhargava, P. K.; Otterby, D. E.; Murphy, J. M.; Donker, J. D.
CORPORATE SOURCE: Dep. Anim. Sci., Univ. Minnesota, St. Paul, MN, USA
SOURCE: Journal of Dairy Science (1977), 60(10), 1594-604
CODEN: JDSCAE; ISSN: 0022-0302
DOCUMENT TYPE: Journal
LANGUAGE: English

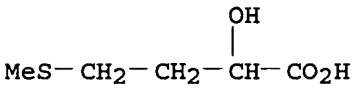
AB In 2 trials in consecutive years 47 and 50 lactating Holstein cows were assigned to grain mixts. that contained 0, 0.1, 0.2, and 0.3% methionine hydroxy analog **[583-91-5]**. Exptl. diets were offered to the cows beginning 2 wk prepartum, and collection of data was begun 4 days postpartum. Alfalfa hay and corn silage were fed ad libitum in a ratio of 1:1, dry basis. Milk fat test and yield were higher for cows supplemented with analog than for **controls** during **early** (4-116 days) lactation. Daily fiber intake was higher for cows fed 0.3% analog (2.2 kg) than for **controls** (1.9 kg) during **early** lactation in y 1 but not in y 2. Milk and solids-not-fat yields did not differ among **treatments.** Intakes of dry matter were not affected by **treatment.** From 117 to 256 days of lactation, there were no differences in yields of milk, fat, or solids-not-fat. Milk from cows maintained on the same **treatment** both y changed little in fat test from y 1 to y 2, but cows that were changed from high analog during y 1 to low during y 2 decreased 0.48 percentage units in test. Those changed from no analog to analog increased 0.34 percentage units in test, and those changes from low analog to high analog increased 0.23 percentage units. Methionine hydroxy analog appears to be a useful supplement for increasing fat test of cows fed relatively high concentrate diets.

IT **583-91-5**
RL: AGR (Agricultural use); BIOL (Biological study); USES (Uses)
(feeding experiment with, on cows, milk fat in relation to)
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 25 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1977:28736 HCAPLUS
DOCUMENT NUMBER: 86:28736
TITLE: Response to nonprotein nitrogen and sulfur sources by the **early**-weaned calf
AUTHOR(S): Winter, K. A.
CORPORATE SOURCE: Res. Stn., Agric. Canada, Charlottetown, PE, Can.
SOURCE: Canadian Journal of Animal Science (1976), 56(3), 567-72

CODEN: CNJNAT; ISSN: 0008-3984
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Calves were used in 2 expts. to evaluate 2 nonprotein N sources and several S sources in calf starter rations. Experiment (1) compared urea [57-13-6] and biuret [108-19-0], with and without methionine hydroxy analog (MHA) [**583-91-5**], and S plus MHA; experiment (2) compared the effect of elemental S and Na2SO4 added to a urea-supplemented starter on calf response to these feeds. Performance of calves on the biuret-supplemented starters was reduced as compared with urea-supplemented starters. The addition of S or MHA to the NPN-supplemented starters did not affect animal performance. However, S did tend to improve performance of the urea-fed calves and had the reverse effect when biuret was fed, while MHA tended to depress performance when urea was fed. In the 2nd experiment, the addition of either S or Na2SO4 to the urea-supplemented starter did not improve animal performance, even when 40% of the total protein in the diets was supplied by nonprotein N sources. The urea-supplemented starter rations had N:S ratios before S supplementation of 11.4:1 (experiment (1)) and 9.4:1 (experiment (2)), close to the ratios considered optimum for ruminants.
IT **583-91-5**
RL: AGR (Agricultural use); BIOL (Biological study); USES (Uses)
(feeding expts. with, on **early**-weaned calf)
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 26 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1965:448290 HCAPLUS
DOCUMENT NUMBER: 63:48290
ORIGINAL REFERENCE NO.: 63:8800f-g
TITLE: The development of an amino acid reference diet for the **early** growth of chicks
AUTHOR(S): Dean, W. F.; Scott, H. M.
CORPORATE SOURCE: Univ. of Illinois, Urbana
SOURCE: Poultry Sci. (1965), 44(3), 803-8
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An amino acid diet patterned after the one reported by Greene, et al. (ibid. 39(2), 512-14(1960)) containing the equivalent of 26.20% protein was modified to give maximal growth with minimal levels of amino acids. The final mixture contained the equivalent of 17.6% protein. Expressed as percent of the diet the composition is as follows: L-arginine, 1.10; L-histidine, 0.30; L-lysine, 1.12; L-tyrosine, 0.63; L-tryptophan, 0.225; L-phenylalanine, 0.68; DL-methionine, 0.45; L-cystine, 0.35; L-threonine, 0.65; L-leucine, 1.20; L-isoleucine, 0.80; L-valine, 0.82; glycine, 1.60; L-glutamic acid, 12.00. All assays were conducted in the presence of 1% proline.
IT **583-91-5**, Butyric acid, 2-hydroxy-4-(methylthio)-
(feeding expts. with, on chicks)
RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)